

The Pathology and Etiology
of
Pulmonary Tuberculosis,
in relation to the
natural method of limitation
of the disease and
the various methods of
inducing artificial limitation.

by

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It is not proposed, in the following pages, to write a critical digest, or even epitome, of the Pathology and etiology of tuberculosis. Such a task would be impossible within the limits of a reasonable thesis, owing to its complexity and magnitude. It is rather my aim to sketch rapidly the features of the pathological process, and the various factors, usually designated etiological and diagnostic, and in the light of the indications derived from them to ascertain the lines along which to work, in order to induce a natural arrest and eventually a complete cure.

The various steps of the argument I originally worked out in the opposite direction, that is, following an empirical line of treatment I set myself to work out, on physiological lines, the rationale concealed behind the complex pathological processes, successfully combated by it. To follow out the argument step by step, is however easier in the former direction and perhaps equally striking. A vast amount of work has been done by many to unravel the numerous pathological factors, which are the primary causes of the various signs and symptoms by which we recognise the disease. Much of our knowledge is still vague, by reason of the experimental difficulties by which work on the subject is/

is surrounded. The extent to which secondary factors enter into and influence the signs and symptoms of the disease does not yet receive the recognition which it deserves. So far with one or two exceptions to be noticed later, the treatment of tuberculosis has been practically empirical, founded on various fallacious interpretations of pathological and clinical facts, which themselves were but little understood. Until quite recently the progress of the disease towards a fatal issue was a sufficiently familiar prospect, while these cases which were treated satisfactorily were either relieved of their disease mechanically or treated by change of climate. In the former the process was rendered incapable of study, inasmuch as the change was sudden and the cure was independent of the effects of nature; in the latter continued observation was usually impossible. Thus the results of treatment were frequently seen, but the gradual development of the process was comparatively rarely studied except in those cases in which progress was in the only too familiar direction. As a case progresses towards arrest of the morbid process the various secondary disturbing factors are gradually eliminated, by appropriate treatment, or by elimination of the various casual influences, and the disease stands out stripped of many familiar features; the/

the inclusion of which in the essential clinical picture has been so fruitfully productive of misconceptions.

When the various signs and symptoms come to be analysed they will be found to be arranged in two groups, as determined by the dual nature of the pathological process concerned. The recognition of this classification is the fundamental guide to the proper conception of the relationship existing between the various groups of symptoms.

Like all organismal diseases, tuberculosis is dependant on two sets of processes :-

(1). The immediate reaction of the tissue of the affected organ to the presence of the invading organism, causing the formation of what is variously termed the essential, local, or characteristic lesion of the disease. This gives rise to various symptoms and physical signs, whose relative prominence depends on the extent of the interference with the function of the organ affected, and the accessibility of the diseased area to the various methods of clinical observation. When the organ or structure involved is superficial, as, for example, in small pox, diagnosis is usually obvious, and dependent on the appearance of the characteristic lesion, and can be made/

made at a relatively early stage in the disease. In proportion as the interference with function on the part of the organ affected is great, so is the size of the space, occupied by the phenomena dependant directly on the primary lesion, large in the clinical picture.

The reaction to the bacillus by the affected tissue in typhoid produces a characteristic lesion which is the essential feature of the disease . This is however, relatively difficult to determine, because the intestinal mucosa in the region affected are not amenable to any of our present methods of examination, and so the diagnosis is made relatively later in this disease than in smallpox, and has to be made by taking various other secondary phenomena into consideration. In pulmonary tuberculosis the local infection and reaction produce certain pathological changes, resulting in the production of the granulomatous growths characteristic of the disease, and capable of detection, when far enough advanced, by certain familiar clinical methods; and giving rise to certain symptoms, e.g. dyspnoea, dependent on the interference with the proper performance of function of the organ affected.

The more difficult the primary lesion is of detection by physical examination, the later, generally, is a certain diagnosis made and the more must the secondary/

secondary signs and symptoms contribute to it.

(2) The second group, into which the signs and symptoms of organismal disease are divided, is that dependent on the absorption and circulation in the body of various products of the metabolism of the pathogenic bacterium, and is consequent on the activity of the primary lesion. These phenomena are directly dependent for their intensity on the virulence and rate of progress of the primary lesion, as indicating indirectly the metabolic activity of the invading organism. They are at first due to functional disturbances of various physiological mechanisms, but in time produce, in a chronic disease like tuberculosis, actual secondary organic lesions which are far reaching in their influence, and serve to complicate the features of the disease. This renders differentiation of the symptoms and signs due to the primary toxic process from these owing their immediate existence to secondary changes well nigh impossible.

In tuberculosis an early, if not the earliest sign of disease is a circulatory disturbance, due to the toxic action on the heart muscle. It is at first functional, but eventually becomes organic, and takes the form of brown atrophy and fatty change, in this way exacerbating the primary cardiac deficiency and rendering it increasingly difficult to overcome/

overcome. As indicated above, if the signs and symptoms of the primary lesion are slight, or developed only at a fairly late stage in the process, the secondary group occupies a relatively important position in relation to early diagnosis, and hence the importance of discrimination between the various pathological factors concerned in their production. The unsatisfactory nature of the treatment of pulmonary tuberculosis has been due, in large part, to this confusion, and the treatment of the local lesion has been neglected, in treating a thousand and one symptoms which are entirely secondary to and dependent on it, or are the direct results of pathological processes set agoing in virtue of its activity. To render "confusion worse confounded," the local lesion in pulmonary tuberculosis is liable to a mixed infection by a variety of organisms, producing their own set of specific symptoms, and setting agoing another series of pathological changes.

Successful treatment of such a disease, which can be used with any amount of intelligence, cannot in the nature of things be empirical. Its application must depend on the ^{recognition of the essential from the} nonessential in the consideration of the pathological processes, concerned in the production of the primary and secondary groups of symptoms and signs and their sequelae.

It must owe its origin to the study of the pathology of the disease on a knowledge of which depends/

depends the proper interpretation of the clinical facts and observations. Such a treatment will be directed to the breaking of the vicious cycle set agoing by the morbid process, not by dissipating its energy on the whole circumference, searching, often vainly, for a weak spot, but by focussing it on the axle on which the integrity of the whole system depends. Such treatment can be intelligently varied as the features of the cases vary, without losing sight of the primary lesion through a mist of secondary symptoms. It will directly aid nature in her efforts to bring about a natural cure, and will not diminish the powers of resistance of the individual by antagonizing any one to another.

It is best therefore to commence the actual discussion of the subject by taking up the pathology, if possible, at the simplest and most uncomplicated stage.

It is impossible to treat such a subject as a whole, so only that part will be considered in detail which appears specially to throw light on the lines along which the efforts of nature are directed, and help to arrive at a conclusion as to the rational treatment of the disease. If the consideration of the subject seem diffuse and ill-arranged the excuse must lie in the infinite complexity of the component factors of the problem, and the difficulty of their differentiation/

differentiation. The series of cases quoted, and on which observations were made, were, during the whole course of treatment, under the writer's direct observation.

A more extended survey of a larger number of cases treated in the Sanatorium, who have been long enough away from direct treatment to justify any conclusions being drawn as to results, is included as an appendix.

The condition in tuberculosis beginning with a simple bacillary infection, accompanied and followed by its double series of results, becomes as the disease progresses more complex.

The primary lesion, running at first a well defined course, becomes later the site of various secondary processes. The cell infiltration of the early nodule undergoes caseation, and at this stage the simple nature of the process is lost. Attempts are made to remove the effete tissue by phagocytosis, which, usually, only serve to restrain the collection of degenerated material to an insignificant degree, and the mass invades a surface exposed to the attacks of extraneous organisms. The surrounding cells, weakened by the general systemic mal-nutrition and the direct local toxin production, become destroyed and then the phenomena of a secondary coccal infection/

infection appear:- superadded to the primary uncomplicated tuberculosis. In the same way the various groups of signs and symptoms are exacerbated and complicated. Early functional disorder becomes organic and a vicious cycle is set up, the toxins of the septic organisms initiating various secondary processes which follow a like course.

To arrive at a conclusion as to the exact nature of uncomplicated tuberculosis, the disease must be studied before these secondary phenomena develop, or after they have been removed by appropriate treatment.

These two epochs at which tuberculosis can be properly studied were rarely previously seen, as compared with the vast amount of complicated disease. The early stages are rarely seen. The onset is insidious. From day to day there is little change in either the primary lesion or the general health. The change is thus not immediately apparent to the patient himself, and he gets gradually accustomed to an indifferent state of health, and forgets how far he has degenerated from a state of physical well being.

It is generally the onset of one of the indications of complications which causes him to consult a physician. It may be, for example, the onset of disintegrative change and the development of a cough and spit which makes him realize that something serious is/

is wrong, but already the disease may be no longer purely tubercular. In the later stages of the cure the complications are again eliminated but the conditions are artificial. Although the pathological processes causing the secondary symptoms have been checked, the condition of the patient is not what it was at the start of the disease. All the systems have been more or less affected by the artificial conditions of treatment and the changes resultant from disease, so that we have no longer got a physiological entity to deal with, whose reaction to stimuli can be predicted with precision, but a more or less modified product of varied conditions and surroundings.

Even although complicating features have been eliminated and the patient restored to the status quo, we still have the features of the disease modified by the treatment, so that this stage is relatively less suitable for studying the exact processes and their results than the earlier stage.

The earlier stages are however often inaccessible directly, owing to the comparatively late stage at which a positive diagnosis is usually made, but many characteristic phenomena may be observed in the history of the individual cases. By taking as wide a survey as possible the earlier features of the disease may be recorded and the relative frequency/

frequency with which certain features occur, and especially, the concurrent existence of certain combinations of signs and symptoms, which are of inestimable value as diagnostic indications. By such means the probable existence of tubercle may be suspected, and a course of treatment ordered on suitable lines which will eradicate the disease when the system is best able to react, besides presenting scope for the thorough investigation of early Tuberculosis.

To arrive at a conclusion as to how far back in a patient's history we are justified in looking for manifestations which may reasonably be set down to the initial prodromal symptoms, we must endeavour to answer two questions :-

1. What is the incubation period of pulmonary tuberculosis?
2. What is the duration of the period of invasion during which prodromal symptoms may occur?

To settle these questions we must determine the date of infection in each case, but it may be stated that, for practical purposes, the division into incubation period and invasion period cannot be discriminated, and the period of invasion may be regarded as stretching from infection to actual definite onset, always bearing in mind that the primary/

primary incubation period is one of relative inactivity on the part of the bacillus.

It is needless for our present purpose, to discuss in detail the various channels of infection in Pulmonary Tuberculosis, but it will suffice to say that, in many cases, a primary infection of the Respiratory Tract involves the bronchial lymphatic glands, and that the main spread of the disease takes place into the lung tissue from the root of the lung. The process probably spreads by direct anatomical continuity chiefly towards the apex. The disease spreads from this centre of vascular distribution radially towards the pleura, and reaches the surface in a large percentage of cases towards the inner end of the 1st intercostal space. One would expect to find such a spread to be strictly radial but for reasons probably functional the mischief spreads as a rule most rapidly upwards. This site, ^{as} being frequently an area of early changes in the breath sounds, has been pointed out previously but my observations tend to confirm it, as a large proportion of my early cases (90%) had changes in this locality.

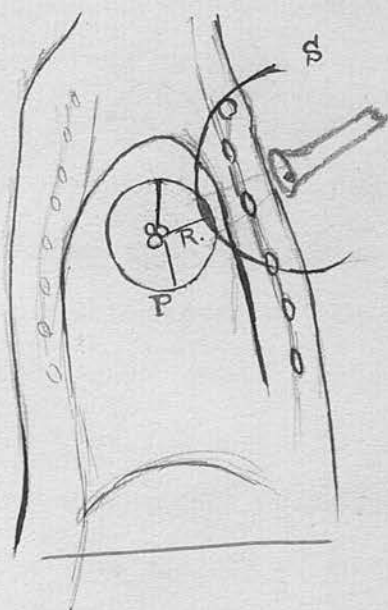
When a physician is called in to examine such a case he finds change of breath sounds over the area indicated or perhaps elsewhere towards the apex. He asks the patient how long he has been ill, and receives/

receives the familiar reply of "a few weeks." He arrives at the erroneous conclusion that this is a slight case of disease of a few weeks duration. He forgets that the process may have, probably did, start at the root of the lung, and spread from that centre outwards towards the pleura. The imaginary extent of the diseased area is simply the arc of a circle whose centre is at the root of the lung and whose radius is the extent to which the mischief has spread radially. The size of this arc is determined by the intersection of another circle whose centre is at the point of application of the stethoscope and whose radius is determined by three factors.

1. The intensity of the conduction outwards of the breath sound determined chiefly ^{by} the diameter of the primary circle of involvement (supposing the lesion to be simple consolidation).
2. Thickness of the nonconducting media, chestwall pleura etc.
3. Acuteness of hearing on the part of the observer.

Diagrammatic/

Diagrammatic anteroposterior Section through the right costal cartilages.



- R.R. Radii along which vessels travel towards pleura from the root and along which lesion spreads.
- S. Circle of Auscultation.
- P. Circle of primary involvement.

Such a simple case as shewn in figure probably never actually exists, as secondary infections and local conditions modify the rate of spread in various directions. It is accelerated by fresh metastatic deposit or devitalization of the lung tissue, and retarded by increased resistance and increased functional activity in any special direction. Still however, the general principle holds good and reveals a serious fallacy in the usual estimation of the duration of the process. In addition it must be remembered/

remembered that, the rate of spread is not by arithmetical progression, so much in a given time and double that amount in double the time, but rather resembles geometrical progression. The rate of spread, *ceteris paribus*, depends on the extent of the lesion already present. The greater the size of the lesion, the greater the toxin secretion, and the greater the devitalization of the tissues, and consequently, the more rapid the spread. The rate, of course, cannot be reduced to Algebraic Formula, but here again the general principle holds good ; that the greater the amount of mischief already present the more rapid the spread. These two principles, or rather, their non-recognition, are the two determining factors in the fallacies one meets with in estimations of the probable duration of ^{the} morbid process in any given case.

If these considerations be true, it is obvious that we must look further back than the usually assigned two or three weeks for the duration of the process, even in the earliest cases. In fixing the precise period of infection it is important to note that, while we may be able to fix approximately the date of a known instance of infection, that does not preclude the possibility of a previous or subsequent exposure. This is an error which is forcibly impressed on us when we recollect the frequency with which/

which the Tubercle Bacillus is found in the dust of rooms, railway carriages, etc. The actual estimate on the subject of the duration of the period of invasion can only be accurate in a very large statistic, and then, at best, can only be approximate. In the series of cases under review the infection where demonstrable was from contact with some sufferer from the disease, in many cases the patient's relative. In such cases exposure to infection is usually prolonged and repeated, so that the exact date can not be fixed. In every case quoted the date has been calculated from the death of the person from whom the infection was conveyed. The error must thus be on the side of shortening the period. Looking at the subject from a more general point of view, the extent to which the spread (as shewn above) must take place before the lesion is demonstrable, and the exact nature of the pathological process one would expect the period of invasion to be long, probably years at the shortest. In the number of cases quoted (60) there was a definite history of exposure to almost certain infection in 31%.

In most cases the period is calculated from the date indicated above to diagnosis when that coincided with admission. In some cases the period has been calculated to the time when weak chest was ventured upon/

upon as a diagnosis, or other symptom, undoubtedly tubercular in the light of the subsequent course, justified a positive opinion. The question as to the period at which diagnosis was first possible is determined chiefly by the acuteness of the observer and this variation in Pulmonary Tuberculosis is found to be of considerable amplitude. All the other errors are on the side of shortening the supposed duration. It is obvious that in such a statistic, an exact estimation is worthless, but it is interesting to note that in the present series it was three years two months. This, for the reasons ^{given} above, is probably very much under the mark.

Were there a primary physical sign characteristic of the disease, as the primary sore in syphilis, then the problem would be rendered easy. The same may be said of primary symptoms, but, although the primary symptoms may be well marked, they are individually diagnostically uncertain, and only certain combinations or groups of them are characteristic, and only have to be recognised in this relationship to raise, in most cases of Tuberculosis, a definite suspicion of the real nature of the malady, and, in well marked cases, when used with common sense and experience thus suffice to decide the diagnosis.

The/

The question of the period of invasion in Tuberculosis and the various prodromal symptoms included therein was discussed by Professor Ruata in a communication to the Medical Annual 1901. p.534 et seq. He cites a case where the patient had been exposed to infection 30 years before he first came under his care in 1898. In that year he had a haemorrhage but examination failed to reveal any physical signs of Tuberculosis. Another haemorrhage occurred about a year later, when definite physical signs were found. He argues that the physical signs took a year to penetrate from the root of the lung to the surface. So far it upholds the contention raised above as to the actual extent of the mischief at the time when diagnosis by physical signs first becomes possible. The case is an unfortunate one for quotation, as a type from which to calculate the duration of the period of invasion, since the patient was continuously exposed to infection for almost seven years, so that the exact date is obscured. He further states that 90% of his cases give a definite history of infection 2-4 years prior to diagnosis. I was only able to obtain definite history, that is, sufficiently definite to be reliable, in 31% of the total cases. Professor Ruata further gives a history of various prodromal symptoms during the period 2-4 years prior to the actual development of physical signs. When however it/

it is taken into consideration that the incubation period is almost certainly a long one, this fact would further tend to antedate the actual date of infection still further. The practical deductions to be drawn from Professor Ruata's Article, in the light of the various statements made above are ;-- that infection may take place an almost indefinite period before the development of physical signs, and that particularly during the last 2-4 years of this period, but in many cases even earlier, the disease has been progressing rapidly and shewing itself in the form of intercurrent attacks of various descriptions. The outcome of this analysis of the invasion period, in the light of previous statements regarding the complication of the tubercular process by its duration, is that in studying the disease with the view of classifying the various signs and symptoms under the various pathological processes responsible for them, we must go back, in many cases, years to reach the root of the evil and see it in its simplest form, unmodified by the artificial conditions induced by treatment, and the secondary symptoms which enter into the clinical picture of the disease as usually recognised.

When we study the prodromal symptoms in detail we see that they are arranged in various trains of increasing/

increasing severity as the disease progresses, each set being referable to a disturbance of the physiological mechanism of a certain system.

They may be conveniently grouped as follows:—

A.. Disturbances of the alimentary system.

(1) Anorexia.

(2) Dyspepsia following on the Anorexia and consequently present at a later date in the life history of the disease and often amounting clinically to a complication.

B. Disturbances of the circulatory system.

(1) Deficient arterial tension with secondary myo-cardial changes.

C. Nervous disturbances. Especially interference with the physiological action of the heat-regulating Centres.

D. Respiratory System.

Passing waves of congestion and disturbance passing through the lungs.

Of these the respiratory groups and the nervous groups are more intimately associated with one another and with the primary condition than are the others.

In cases where the tubercular element is not recognised, these conditions are given various names, popular and scientific. The disorders of the alimentary tract are:- anorexia, dyspepsia and Constipation. These are such common features of non-tubercular/

non-tubercular disease as to be individually of no significance. They are here essentially toxic in origin. The condition commences with anorexia which passes into constipation and dyspepsia. This is treated with milk diets and carbo hydrate food which tends to aggravate both the symptoms and the activity of the local lesion. The constipation is due in part, to a faulty alimentary chemistry, but chiefly to a depression in the excitability of the intestinal muscle. This muscular condition induced by the circulating toxins produces symptoms in all the bodily systems whose function is performed in whole or part by muscle. It induces the cardiac deficiency which is so characteristic of the circulatory conditions in tuberculosis. Whether the actual histological changes in the cardiac muscle, brown atrophy and fatty change, is due to this early toxaemia or to the later septic poisoning is uncertain, but this much is certain, that circulatory debility characterizes the initial stages of the disease. To this general muscular condition is probably due, in great part at least, the feeling of languor and unfitness for work so often complained of. This is usually attributed vaguely to the Dyspepsia, but it seems a needless complication to introduce a new disease to explain every additional symptom, when the single condition of toxaemia exists, and, from what we know of the directions of/

of its later action, is amply sufficient to explain the whole chain of prodromal symptoms. The common characteristic of all the early symptoms of the disease is, that they are functional and quickly yield to treatment. When however the condition has gone on for long, and organic changes have set in, the conditions assume the obstinacy of ordinary dyspepsia of primary gastric origin, or other disease of the affected systems. The longer recognition of the true state of affairs is put off, the more obstinate the symptoms become and consequently the worse is the prognosis. The respiratory conditions have a somewhat different significance. Here we have to deal with the organ in which the primary lesion is presumably situated, we have to do with a tissue, part of which is diseased. The consequence is that the extraneous organisms causing various catarrhal conditions of the respiratory tract find entrance with greater ease than normally, and consequently we have a frequent history of liability to colds etc. The conditions, classed as such, are by no means all colds in the ordinary sense. The area affected is limited, constantly we hear of patients having colds with 'catarrh at one apex' or 'localized bronchitis.' Colds properly so called are not limited. A bronchitis is practically never found/

found limited to one lobe or one lung. They invade normally the whole respiratory tract, from above downwards symmetrically, and their severity depends on the extent downwards to which the mischief penetrates. The condition ^{penetrates symmetrically.} It may begin as a Pharyngitis or coryza and travel downwards, laryngitis follows and then bronchitis. The bronchitis may, at the moment of examination, be more marked in one lung than the other but is always bilateral and generally involves the whole bronchial tract, i.e. rhonchi and crepitations are heard practically over the whole chest wall. In tubercle the condition is different, the râles are generally localized, often very much so. So called "catarrh of the apex" is simply another name for early Tuberculosis. It is probably the surface indication of the condition described microscopically by Baumgarten (B. Tuberkel und tuberkulose, section on lung).

The deposit of tubercle is followed in the lung as elsewhere by a local reaction of the pulmonary cells before the lymphocytic invasion takes place. So marked is this, in the lung, that whole areas of partially consolidated tissue retain the alveolar walls and look like a catarrhal pneumonia. The whole is later overflowed by a flood of leucocytes and the histological arrangement is obscured. Such/

Such is the condition of a lung with so called apical catarrh. The condition is distinguished from a catarrhal pneumonia with difficulty but the main indications which point to tuberculosis are :-

(1) The small area involved; (2) The relative slowness in the development of physical signs; (3) Intermittency of the moist sounds, sometimes disappearing altogether, to return again directly a fresh infection causes a coryza and general catarrh devitalizing the pulmonary tissue and giving the tubercle Bacillus the opportunity of committing fresh ravages; the coryza and general catarrh disappears in a few days but the localized patch remains permanently or disappears more slowly; (4) Relatively slight constitutional disturbance as compared with true catarrhal pneumonia. It will be observed that the distinctions are only those of degree, early tubercular catarrh is simply a catarrhal pneumonia. An exacerbation may be initiated by catarrhal organisms, but the tubercle bacillus always affects the stages of the disease in the direction indicated.

Localized more or less persistent catarrh is always to be regarded with the suspicion as possibly early tuberculosis. The same differential features apply to the pneumonias at this stage. Some may be true pneumonia, but a suspiciously large number have the history/

history of 'not clearing up properly', 'no crisis' etc.

Such conditions may obtain in true pneumonia, but, in association with others of the prodromal symptoms, are always, to say the least of it, suggestive.

Pleurisy in such cases is similar in every respect, but perhaps even more to be regarded with suspicion as will be seen on inspection of the tabular statement given below. Haemorrhage, although in 99% of cases of so called idiopathic haemoptysis, is really the result of tubercular erosion, is included in the detailed statement. Apart from history of effort or strain or obvious bleeding points in the upper respiratory passages, haemorrhage is perhaps the gravest sign from the point of view of diagnosis of the condition. Recurrence even without physical signs especially after long intervals, is in most cases amply sufficient to clinch the diagnosis. Gastric haemorrhage must of course be excluded, by careful examination of the blood and a comparison of collateral symptoms and physical signs.

The only other condition requiring special reference is influenza. This diagnosis will be seen to be exceedingly frequent. No doubt it includes cases of true influenza, but it is significant that not in a single case was the diagnosis confirmed bacteriologically, as far as could be gathered from the patients or their friends. I have seen numerous cases/

cases of acute pyrexial attacks resembling influenza but only on two occasions was I able to demonstrate the specific bacillus in the blood or sputum;

otherwise the condition was indistinguishable from true influenza. The causes of the temperature will be discussed in full later, but at present it will suffice to say that exaggerated response to stimuli is the characteristic of the action of the heat centres in this disease. An ordinary cold which in a normal person causes slight pyrexia 99-100, in a case of latent tuberculosis, living under normal conditions, produces a temperature curve indistinguishable, in some cases, from that of true influenza. I have on several occasions observed in the blood during or previous to such an attack a coccus but only twice have I found the specific (Pfeiffer's) bacillus or any organism remotely resembling it. The condition is not very different from true influenza but the special symptoms are less marked.

Prostration, pains and catarrh are either individually ^{are} absent or _A only very slight. The diagnosis in every suspicious case should be confirmed bacteriologically, where possible, especially in recurrent attacks with suspicious associations. Here again the tubercle bacillus influences the type of disease in the direction of diminished acuteness of the characteristic/

characteristic symptoms. The pyrexia has associated with it increased pulmonary signs, but rarely increased change in the breath sound and never anything, in my experience, approaching pneumonia, although slight basal effusion is fairly common.

On the whole, the more mixed the train of preliminary symptoms is, the more is the existence of latent tuberculosis to be suspected.

Whatever the train of symptoms which characterizes the early period of invasion, similar features occur in a modified form during treatment. A case in which the dyspeptic symptoms predominate will remain a gastric case all throughout. Similarly in cases of influenza, the periodic rises of temperature, classed as such before the diagnosis, are found to continue in the form of temperature waves, shewing all grades of curve from that indistinguishable from true influenza, or less acutely, like that of ordinary typhoid, to an intermittent daily swing. The intermittent daily swing is not recognised because the practitioner sees the cases rarely before mid day or afternoon by which time the temperature has risen from the low morning level and approaches the morning remission of a typhoid that has begun its lysis.

Such is a short account of the various prodromal symptoms and the diseases which they resemble or are commonly /

commonly confounded with. The special features which I have endeavoured to emphasize are the tendency to recurrence, and the association of two or more of the symptoms in characteristic groups and sequences, which should suffice to excite the suspicions of the medical man, that he has a case of tuberculosis to deal with, not latent in the usual exact significance of the term, but active, giving rise to few or no signs and symptoms due to the first class of signs and symptoms of organismal disease, and therefore having to be differentiated ^{by} the more vague indications of the second group. The importance of these must thus be recognised, and they should be subjected to careful scrutiny and verification by expert bacteriological and other tests.

The reader must judge for himself how far the appended tables justify these conclusions. The special groups of symptoms will be discussed after the figures are given.

TABLE I.

1. Anorexia	occurred in	98.4%
2. Dyspepsia	" "	83.4%
3. Influenza	" "	51.6%
4. Pleurisy	" "	46.3%
5. Liable to colds	" "	38.3%
6. Haemorrhage	" "	26.6%
7. Bronchitis	" "	16.3%
8. Inflammation	" "	8.3%

The conditions referable to toxic poisoning of the muscular system are omitted from the table but it may be mentioned that constipation, of greater or less severity, occurred in 70-80 % of the cases. The pulse on admission was up to par in no case, but, of course, no history could furnish a statistic of the exact state of the circulation prior to diagnosis. The diagnosis of each of the conditions is that given by the patient, in most cases being the report of the physician attending the case.

The previous table gives the percentage of cases in which any symptom occurred at least once.

Anorexia was a constant symptom and never really absent, but of the more acute symptoms or diseases the following table gives the relative frequency of recurrence.

TABLE II.

CONDITION	PRESENT IN	RECURRENT IN
Influenza	51.6% of the cases	35.5% of these
Bronchitis	16.3% " " "	71.4% " "
Inflammation	8.3% " " "	20 % " "
Pleurisy	46.3% " " "	3 % " "
Haemorrhage	26.6% " " "	75 % " "

Pleurisy/

Pleurisy tends to occur late in the disease being the result of spread from the root of the lung to the pleura; it therefore does not appear in the above table as recurrent to any great extent.

As regards the association of symptoms, it is needless to give further tables to demonstrate the fact, that several of the conditions must occur in association. The high percentage of those affected, at one time or another, with the various conditions necessitates the concurrence of several of them in individual cases. Of these the most important are the digestive disorders. An association of Anorexia, perhaps more than an association of actual dyspepsia, with any of the others is significant. Dyspepsia, associated with various conditions, is exceedingly common in non-tubercular people, but the anorexia and languor, without actual dyspepsia, are especially characteristic of the chronic nature of the tubercular process. The toxaemia is, at first, not sufficiently intense to produce dyspepsia but the tone and appetite are never up to par.

By the time actual dyspepsia supervenes the pulmonary condition should be capable of detection by an acute observer. When any of the more acute manifestations e.g. influenza is associated with intervening anorexia suspicion of the true nature of the/

the case should be aroused. Recurrent pulmonary manifestations are particularly significant, and should be examined carefully, with the view of detecting unusual or anomalous features in the condition, pointing to its not being a pure case of the individual disease, but rather an engrafting of the typical condition on the more susceptible tubercular subject, or a tubercular exacerbation. If this were fully recognised and cases presenting anomalous or suspicious features underwent a course of appropriate treatment it would do more toward the extirpation of tuberculosis than any amount of legislation.

In surgery, it is a routine practice that if the diagnosis of a tumour be doubtful it should be cut into and examined. Should it turn out to be simple, no great harm is done, while, should it turn out to be malignant, the patient may be saved, because here, as in tubercle, it is only in the early stages that diagnosis is, as a rule, difficult. If the same rule were applied to cases suspected of tuberculosis, hundreds of lives would be saved as it is abundantly proved by experience, that the severity of intercurrent attacks of influenza and the other diseases, that are apt to be confounded with the initial manifestations of tuberculosis, is greatly mitigated by open air treatment.

In/

In the cases of undoubted intercurrent organismal disease occurring during treatment and associated with the presence of organisms, including Pfeiffer's bacillus, the constitutional effects following the disease were conspicuous principally by their absence, or diminished severity, even although, in every case, the patient was suffering from old standing tuberculosis. This is in marked contrast to the current opinion as to the seriousness of intercurrent influenza, especially in its relation to ultimate prognosis. Here again the question arises how many of the cases have had their diagnosis confirmed bacteriologically and how many were really tubercular toxic exacerbations of various kinds?

Some of these various conditions will be discussed later in relation to the nature of the tubercle toxins.

So far the consideration of the subject has led us to various conclusions regarding the nature and course of the disease which may with advantage be briefly recapitulated.

- I. The period of invasion in pulmonary tubercle is long, the actual length is uncertain but amounts to several years.
- II. The actual extent of the lesion at the earliest date diagnosis can be arrived at is greater than is ordinarily supposed. This is fully borne/

borne out by post mortem experience. The lesser degrees of pulmonary tuberculosis are frequently discovered for the first time and even where actual diagnosis has been made, in life, the conditions indicated in the 'case' do not correspond in degree with those actually found post mortem.

- III. The symptoms during the period of invasion are intermittent but correspond exactly with the more severe symptoms of the later stages of the same case. This is a noteworthy feature in every case, when the history is compared with the facts observed during treatment.
- IV. The importance of early diagnosis by the recognition of the groups of prodromal phenomena, even tentative diagnosis, and the active treatment of suspected cases.

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Having glanced rapidly over the symptoms which characterise the preliminary stage of the disease and shewn their complexity it is hardly necessary to say that, without the recognition of the primary toxæmia, it is impossible to devise a common treatment for all the manifestations, and that such a treatment must owe its existence to their recognition.

The next question which arises is :-

What is the pathological nature of the change which is/

is the characteristic lesion of the disease and what indications do we have of any efforts of nature to bring about a cure? The histological changes brought about in the tissues by the action of the tubercle bacillus were fully studied by Baumgarten, and published by him in the form of a book,

"Tuberkel und Tuberkulos ." 1885.

His method was to inoculate the Iris of a series of rabbits and note the progressive changes local and general. The inoculation was followed by infection of adjacent lymphatic glands, and then became general. According to his observations, the introduction of the bacillus into the tissues is followed by a series of changes, induced by the action of the specific toxins and to an insignificant extent by their physical presence as foreign bodies. The immediate action of the toxins is to produce a cellular devitalization, the later stage of which is known as caseation. This devitalization and subsequent necrosis is the essential toxic feature of the local disease. The other phenomena which occur are doubtless also due to the toxic action but are, ^{in my opinion} really of the nature of a reaction. Were there no toxic process these other phenomena would not occur, but the effort or energy put forth in their production is not derived from the bacillus but from the tissues; dependent/

dependent on the primary toxic stimulation. They are, in other words, protective and their object is the limitation of the necrotic process. The actual secondary phenomena are not therefore identical in all tissues varying with the nature of the tissue concerned in their production, in marked contrast to the uniformity of the caseous process.

The relative prominence of the different factors depends on the toxic concentration or the rapidity of their production. The first feature of the process in the formation of the tubercle nodule is a reaction on the part of the cells of the affected tissue.

Under the devitalizing influence of the toxin they follow the law that cells in a depressed condition of vitality tend to multiply. They undergo mitosis and proliferation forming a nest round the bacilli.

Were toxic action to cease here the local cells would probably suffice to encapsule the intruding bacilli but this never occurs. The toxic action is in excess of the immediate reaction and ends in the swelling and hyaline degeneration of the adjacent cells. This proceeds eventually to caseation.

The condition of affairs at this stage is, that there is a nodule of dead or dying cells in the tissues, from which emanates a double series of stimuli.

There is the primary stimulation of the presence of a foreign body inducing a chemiotaxis exerted on cells/

cells having a phagocytic function. There is therefore a local accumulation of polymorphonuclear leucocytes. The nodule from a physical point of view is small and the resultant reaction is slight, therefore the polymorphonuclear infiltration is slight and does not cause a pathological leucocytosis, especially as the condition, unlike acute suppuration, is very gradual. There is however a second stimulus given out by the nodule. The bacillus having conquered and killed the surrounding tissue cells is now actively secreting its specific toxin,
 I hold
which exerts a chemiotactic influence on certain
specific cells which invade the periphery of the
nodule, far outnumbering the polymorphonuclear
leucocytes. These cells are the mononuclear
leucocytes, or lymphocytes, While the polymorpho-
nuclear leucocytes are attracted in virtue of their
phagocytic capabilities by the presence of any
foreign body, the lymphocyte is capable only of
attraction by specific toxins or the bodies produced
by the metabolism of certain pathogenic bacteria
of which the tubercle bacillus is a type. The
 nodule at this second stage consists of the central
 dead or dying deposit of cells surrounded by a zone
 of cells, called in from the system generally by the
 above chemiotactic actions. Of these two classes
 of/

of cells the lymphocyte is in large excess as compared with their relative numbers in the blood, where the polymorphs roughly aggregate 70% of the total.

The slower the toxic secretion or rather the less the excess of toxin over the production of neutralising bodies by the cells, the slower is the caseation and the more perfect the histological changes of protective significance in the local tissue cells, and the later does the chemiotaxis take place thus summoning the aid of the general systemic cells.

The tubercle nodule is too commonly regarded as the direct product of the tubercle bacillus. The nodule is the product of the tissues solely, and constitutes the barrier which nature raises to limit the disease. It is not strictly speaking a new growth as only the early proliferative changes are of the nature of a new growth, and they form only a small part of the typical nodule.

* Since writing the above, a paper by Barbain (Centralb. f. Allgem. Path. Bd. XIII 2 1. B. M. J. Epitome April 4th 1903 No. 232). He describes an initial phagocytosis by polymorphonuclear leucocytes at the point of inoculation. This is followed by the lymphocytic infiltration the cells of which 'persist in spite of the bacilli' indicating their antagonistic position. 'Occasionally' polymorphonuclear leucocytes invade the caseous nodule removing the detritus (see criticism of cinnamic acid treatment below. p. 110)

The invading cells never shew mitosis, (Baumgarten) and therefore are to be regarded solely as the local accumulation of wandering tissue elements, consequent on a specific series of chemiotactic attractions.

If the consolidation, to give it its clinical name, were the product of the tubercle bacillus in the sense it is often regarded, then the greater the amount of infiltration (not caseation) the greater would be toxic secretion and systemic disturbance; but the reverse is the case. One of the first evidences of a local reaction to treatment is an increase of the intensity of the consolidation over an area smaller than that occupied by crepitations i.e., the 'area of catarrh', and consequent general improvement, with however more definite local physical signs of consolidation. In Bovine tuberculosis where, either the bacillus is modified by the occurrence of the disease in a different species, or the local reaction tends to be more perfect, large masses of infiltration are found on the serous surfaces with no systemic deterioration. This may in part ^{be} due to the fact that the serous surfaces are not vital organs and therefore interference with function is less, but that does not explain away the fact that huge masses of tubercle nodule co-exist with little or no toxæmia. This shews that the nodule is the result of a gradual toxic action accompanied by constant neutralization/

neutralization, so that the systemic toxæmia is always kept within bounds by the local action.

In strong contrast is the condition in human caseous pneumonia, where the amount of cell infiltration is small, relatively to the total area of the lesion which consists of huge caseous masses with extreme toxæmia and symptoms, temperature, sweating, wasting, muscular enfeeblement, cardiac and skeletal, in fact all the toxic phenomena which, in a lesser degree, we have endeavoured to associate with the prodromal stage of the disease, are exceedingly acute and the disease runs a rapid course, dependent on the poisoning.

Here the local condition is a wider-spread local tissue proliferation, resembling histologically, a catarrhal pneumonia, followed by a similar rapid caseation with either too little time for a round cell infiltration to take place efficiently, or a bad reaction on the part of the tissues concerned in the production of the infiltration. The disease spreads in single lung-areas, as opposed to miliary tubercle, where the disease spreads from ^{an} innumerable number of metastatic foci. How the sudden spread has taken place in the latter and how the simultaneous lodgment of bacilli in widely separated parts of the lungs and other organs ^{has occurred,} has not been satisfactorily explained. Each focus has its own series of phenomena/

phenomena. Each nodule has to be separately inclosed by a zone of lymphocytes to prevent systemic poisoning by the extra cellular toxins of the bacillus. This entails an extra amount of infiltration as, obviously, it requires more cells to encapsule a large number of separate small foci than were the total amount of toxic secreting tissue aggregated in a single area. Were there only a single focus, the condition would approximate to ordinary tuberculosis, and a smaller number of lymphocytes suffice to induce an arrest of the process. This is probably the explanation of the rapidity of spread of the form known as miliary as opposed to ordinary tuberculosis. The condition is acute and there is considerable systemic disturbance, but on different lines from caseous pneumonia. In miliary tuberculosis there is relatively little caseation and practically no breaking down. The condition is not due to the want of reaction but to the great toxic action induced suddenly, placing as we have shewn, the cells producing the reaction at a disadvantage. The symptoms are therefore those of functional interference, rapid shallow breathing combined with a relatively pure tubercular toxaemia. It is significant in this relation as will be seen later that cases of undoubted miliary tubercle occur with no elevation of temperature. In caseous pneumonia/

pneumonia on the other hand, there is invariably a high temperature. The process is not purely tubercular the caseous area is the site of processes the result of mixed infection and the various signs and symptoms indicate acute systemic septic poisoning superadded to the primary tubercular element.

The next point to take up is the exact method of the toxic action of the tubercle bacillus in producing the nodule. The degeneration of the tissues is probably caused by an intracellular toxin and not a body excreted into the circulation. Caseation and the nodular phenomena never occur apart from the presence of tubercle bacilli, even where there are evident symptoms of systemic toxæmia. That is, the poison concerned is contained in the bodies of the bacilli. It has been shewn by Prudden and Hosenpys and others that the dead bacilli injected into the circulation produce nodules similar in structure to the ordinary nodule with this distinction that caseation never takes place except when the dose is very large and the quantity of intracellular toxins present is sufficient to produce this final stage.

New York Med.Rec. 1891 page 34.

The study of the typical tubercle nodule as originally propounded by Baumgarten shews that the essential/

essential distinguishing feature is the lymphocytic infiltration. The lymphocytic infiltration is a chemiotaxis exerted on various cells by certain extracellular toxins or other bodies produced in the metabolism of the bacillus in the tissues. It is not a local production because there never is any sign of mitosis in the small round cells.

Seeing that the lymphocyte is the specific cell concerned in the process it is of interest to note the characteristics of tuberculosis of lymphogenic tissue.

Lymphatic tubercle is exceedingly frequent. Without going into statistics on the subject it may be said perhaps to be the commonest form either alone or as part of a more general infection. It takes the form of tubercular lymphadenitis, *Tabes Mesenterica*, or tuberculosis of the bronchial glands in the course of pulmonary tuberculosis. The relative frequency of the disease is explicable when we consider the function of the glands. Their primary function is to act as filters on the course of the centripetal lymph stream. Take the Mesenteric glands as an example. They are situated on the lymph trunks arising from the intestine throughout practically its whole length. The total length of the intestine is, let us say, roughly 25 feet with an

an average diameter of say 2 inches. This gives a total area of roughly 450 square inches in direct lymphatic continuity with this series of glands.

Any gross or molecular^{lesion} of this huge surface which permits of the entrance of extraneous organisms is morally certain to infect one or more of the glands of the mesenteric series. If we do not find cases of organismal infection of this group of glands it is not for want of organisms on the surface drained by the lymphatic trunks. Similarly the cervical glands are exposed to infection from the scalp, teeth and tonsils all of which are septic areas. It is interesting to note that Watson Cheyne Harveian Lectures Dec 99. (Lancet of British Medical Journal December 16th. et seq.) discussing the subject of glandular tubercle, simply from the point of view of Etiology and Surgical treatment, with no special reference to any special antibacterial action of the glands, says that in cases of tuberculosis of the cervical lymph glands the bacilli do not obtain entrance at the original point of inflammatory infection, teeth, tonsils etc, but the tuberculosis is secondary to a nonspecific inflammation of the glands, and a subsequent infection by the tubercle bacillus of the devitalized and therefore improperly functioning glands. 'In a large proportion of cases the/

the battle which ensues between the bacilli and the tissue cells is long; but the latter are finally successful and we find in the calcified remnants in the bronchial and mesenteric lymph glands evidences of victory.' Osler. Medicine page 225. This proves a relatively greater tendency to spontaneous cure than is found in relation to ordinary tuberculosis.

According to Baumgarten (Tuberkel und Tuberkulos: Lymph tubercle .)

tubercle of the lymph glands is essentially similar to tubercle elsewhere with the exception that there is less cell proliferation and infiltration than in primary tubercle. This is precisely what we should expect if the specific antagonistic cells are on the spot ready to take up their antibacterial action. Further, he states that caseation is slower than elsewhere, (i.e. toxic excess is less than elsewhere), while the bacilli themselves decay and are destroyed at an earlier stage than in ordinary tuberculosis, where they remain long living and active in the caseous area. It is also a significant fact that glandular disease was the last strumous affection which was definitely recognised as tubercular ; from the difficulty of cultivating or detecting the specific bacillus in the caseous matter.

The experiments of Arloing and Lingard shew that it/

that
it is with relatively greater difficulty, infection of guinea pigs and rabbits can be brought about when glandular tubercle is the form employed, and that when once established, the disease tends to be less severe and more chronic. It causes death in guinea pigs in from six to seven months, while similar animals died in half that time when inoculated with infected tissue other than glandular (Osler Principles and Practice of Medicine 1897 p.225)

Similarly it is well known that tabes mesenterica and lymphadenitis may lead to the formation of huge masses of tubercular material, producing great deformity, not going on to absolute disintegration and pus formation, (Watson Cheyne Harv. Lect) as would tend to occur to a mass elsewhere, although the mass is by reason of its situation prone to attacks from the septic organisms that determine the occurrence of disintegration of caseous material elsewhere.

Baumgarten holds that the special characteristics of lymphatic tubercle are due to the fact that the infection is produced by a relatively small dose of bacilli. The smallness of the dose is due to the fact of the deposit being metastatic and taking place through a lymphatic channel. This may to a certain extent be true of experimental tuberculosis where the lymphadenitis is secondary to a small tubercle in the iris but does not hold universally. The/

The fact that the dose of bacilli which produces the initial glandular lesion, being small does not exclude the possibility of numbers of subsequent small infections which may form a substantial total.

If the explanation of the characteristics of lymphatic tubercle was the smallness of the dose of bacilli, dissipated and diminished by having to pass through the lymphatic vessels to the gland, then the same features would be common in a greater or lesser degree to metastatic tubercle of any organ. Whatever the mode of infection, whether blood, air or lymph the tendency would be for the dissipation of the bacilli in the passage. In fact in a lymph gland the infection would tend to be relatively great as it has many convergent lymphatics each of which would convey its quota of infection, the whole representing the total infection possible from the area drained into the gland. In conveyance of the infection by arterial blood or air the reverse conditions obtain. In tuberculosis all deposits, except those in direct anatomical continuity with the primary area, are in a greater or lesser degree metastatic yet we do not find that they are characterized by any paucity of bacilli in the lesions, or defective caseation. The conclusion one is bound to arrive at is that the special characteristics of this single tissue are not due/

due to any differences in the virulence or numbers of the invading bacilli but must be due to some specific property of the tissue in question, in the direction of greater resistance to the production of the local toxic action of the bacillus. That, in fact, lymphoid tissue, while being of all tissues the one most exposed to infection is the one in which the essentially toxic effects of the lesion are the most slowly and imperfectly produced. The only exception with which we have to deal is the spleen. In miliary tubercle of the spleen in young subjects (Muir and Ritchie Bacteriology page 228.) we get lesions containing large numbers of bacilli. The spleen is not simply a lymph gland although it contains nodules of lymphoid tissue and cannot be fairly judged by the same standard. It is also noteworthy, that it is at the stage in its life history that the spleen has special functions to perform apart from those of an ordinary lymph gland, that this condition takes place. In addition the miliary type of disease places the lymphoid tissue at a disadvantage as shewn above. It is also possible, if indeed not probable that the sudden spread, apart from the question of its dissemination and distribution by the erosion of veins or large lymphatics, is associated with a sudden fall in the powers/

powers of resistance produced by a sudden toxic access occasioned by the lodgment of many bacilli on relatively defenceless tissue, normal tissue forms a relatively more suitable pabulum for their growth than the infiltrated area they have just left. The fall in resistance may be considered to be as much a failure in general systemic nutrition, which must be considered in treatment as only secondary in importance to the histological limitation of the primary lesion.

In Baumgarten's work I have not been able to find any special reference to metastatic tuberculosis as having any of the above characteristics. One would expect to find that metastatic tubercle would rather have the opposite characteristic features, tending to an exaggeration of the toxic features, as occurring late in the disease when the nutrition and power of resistance have been broken down by a long primary tuberculosis. In such a case we should expect to find the accumulating secondary sequelae

well marked, and in consequence, the systemic metabolism far perverted and the powers of resistance and reaction low, with, as a result, a large number of bacilli in the lesions. That part of the process of formation of the tubercle nodule which tends to vary most is the primary reaction of the tissue cells. This varies as one would expect with the tissue involved/

involved. The only one of special interest from the present point of view is the lung. Here the proliferation of the alveolar cells forms a large part of the early consolidation. It appears like a catarrhal pneumonia shewing the alveolar septa until overflowed by the flood of lymphocytic infiltration. (Baumgarten) This is probably the condition present at the root of the lung when prolongation of breath sounds and crepitations, the so called catarrh, indicate its spread into the tissue of the lung at the immediate apex.

The immediate sequel to the lodgment of the bacillus in the tissues is the formation of the tubercle nodule just described. In this process a double series of toxic changes are initiated. The one is the local necrotic change (Koch) due to the action of an intracellular toxin, capable only of acting within a limited radius of the body of the bacillus. This toxin is complex in its nature. It produces the typical caseous change and is the active agent in the chemiotaxis exerted on the lymphocytes. This action only takes place in the direction of the tissues being devitalized by the immediate presence and metabolic activity of the bacillus. It is not found to act in relation to the extra-cellular toxins. These circulate in the blood and lymph, but a general systemic lymphocytosis is/

is not characteristic of the toxæmia. Whether the actual chemical body producing the caseation is identical with the body producing the chemiotaxis cannot be said with certainty, but so much can be said:- that they are always associated. We know that tubercle does not belong to the groups of organismal diseases in which the production of antitoxin is simple. Besides the toxin of the bacillus being complex and containing many active ingredients whose action is independent of one another, the formation of the antibody for each constituent is itself a complex process. It entails the presence or formation of a second body, called by Ehrlich an amboceptor. This complexity renders the induction of an artificial immunity impossible, in the sense in which it can be produced in Diphtheria and Tetanus.

Welsh (Huxley Lect 1902 Lancet)

The production of the complete active body whether it be toxin or antitoxin is the result of the formation of two bodies, the one produced by the bacillus, the other by the local cells. Something of the same sort probably takes place in the tubercle nodule. The chemiotaxis resulting in the local accumulation of specific cells is secondary to a metabolic change in the local tissue cells. In some tissues e.g. lung extensive local changes may take place before the lymphocytic/

lymphocytic infiltration occurs. The two processes are distinct but at the same time the second is the direct sequence of the first. Of the two the infiltration always occurs second. If the body producing the chemiotaxis is present as such, in the bacillary toxins the two would occur simultaneously or their order might even occasionally be reversed.

Baumgarten however repeatedly affirms.

(Tuberkel und Tuberkulos) in every section of his work that the initial stage of the process is always a change in the local tissue elements seen histologically as a proliferation, resulting in the formation of lymphoid cells, and eventually of giant cells. This would point to the production of a third body produced in the process which is itself the chemiotactic agent either alone or in union with one of the toxic agents, in which case it would correspond to an amboceptor in Ehrlich's side chain theory. The chemiotaxis acting on the polymorphonuclear cells is secondary in importance and is merely due to the local presence of necrotic and irritative matter in the tissue, the result of cell death and is only seen when that has actually taken place. It is in no sense specific and does not require for its explanation the production of a specific chemiotactic agent, as the invasion of a tissue by phagocytes takes place on the introduction of any foreign matter, and the body which produces/

produces it, at least, as far as the casual agent is concerned, is not specific. The phagocytic process is not useless, but only usually tends to lessen the accumulation to an insignificant extent.

Koch's[?] tuberculin both the old and the new is a product containing the intracellular toxins of tubercle which possess a local action.

Without going into the well known details as to its production it may be said that the new tuberculin T.R. is a product whose constituents are more constant in relative proportion than the old T.O. besides being more diluted and containing all the bacillary constituents in a state of true solution. The result of its introduction into the circulation is an increase in the local toxic action resulting in the caseation, en masse, of the devitalized centres of the nodules. Where these have access to a surface an increase of sputum is the result, leaving behind more healthy infiltrated areas to contract, with no central substance to secrete toxin and hinder contraction by its physical presence. The bacilli are not killed in the process and here T.R. as a curative agent fails. If a dose could be given in any case sufficient in quantity and so arranged as to its distribution through the lung, as to cause caseation of the devitalized tissue which could be extruded/

extruded, en masse, as sputum then it might be called curative. This does occasionally happen and the result is beneficial, but if the dose be too great in quantity then the necrotic process spreads to the lymphatic zone and, the bacilli not being killed by the action, the disease is free to spread. The injection of T.R. is followed by a leucocytosis .

This is the effect of the direct increase of necrosed tissue causing an attempt at its removal by phagocytosis. It probably is also due to the increased scope afforded to the local septic processes in the necrosed tissue leading to an increase of the leucocytes. A certain increase is invariably present in cases with vomicae. Probably both these processes come into play in the production of the post tuberculin leucocytosis.

Those, who hold by the view of Metchnikoff that the rôle of the polymorphonuclear leucocyte is phagocytic, will hold by the former, while those, who hold that their function is the secretion of antibodies or haptophore groups, will hold by the latter. The phagocytic element is denied by Baumgarten, while its importance is emphasized by Landerer, as will be seen when his cinnamic acid treatment comes to be discussed. Probably both views are true in part. The unsatisfactory element in the T.R./

T.R. treatment is that its success depends on certain anatomical relations of the disease on which depend the extrusion of the diseased area. The sudden toxic increase caused by the injection will cause, in addition to caseation, an increased formation of antibodies either directly or through the medium of increased lymphocytic infiltration, provided that there is a residual capability for reaction on the part of the patient which can be called into active exercise by an increased stimulation. The increased stimulation passes off suddenly as it came, leaving the reaction in operation. Should such a series of phenomena be pleased to take place in their proper order and to their proper relative ^{extent} the effect on the disease amounts almost to a cure. If however the anatomical conditions are not present there is an increased area of dead tissue containing an excess of toxin. This affects the surrounding consolidation allowing the bacilli to get to work with increased vigour. Should the requisite physiological power of reaction be present, it may neutralize the toxic excess and prevent spread without definite improvement, but should it be absent, toxic poisoning with no neutralization by antibodies takes place, causing secondary spread.

The treatment is an attempt to get rid of the foci, which may be an anatomical impossibility and to /

to cause increased secretion of antibodies, which may be already taking place to the utmost physiological capacity of the individual. Where the lesion is superficial as in lupus or tuberculosis of the air passages the principle is sound and the results often good. Where the lesion is not superficial, and the power of reaction not present, the reverse may be the case. The measurement of the capability of the individual for reaction has not yet been made possible and can only be estimated roughly by the state of the general health. In short, cases where T.R. is beneficial are those which are obviously suitable or cases which would recover without it, and the artificial hastening of whose recovery is attended with risk.

Such is the rationale of the T.R. treatment and the reasons accounting for its nonsuccess. It has been introduced here because it can be more conveniently followed in relation to the discussion of the toxic effects of tuberculosis.

Alongside of the series of primary toxic changes caused by the intracellular toxins of the bacillus, there is the second group of disturbances caused by the extracellular or circulating toxins.

These are mainly evidenced by functional disorders of various descriptions. As soon as the disease obtains/

obtains a footing and caseation occurs, this general systemic toxaemia sets in. It is at the bottom of all the symptoms and signs which occur during the so called period of invasion, referable to the various systems affected by the toxins during the actual course of the disease. The chief characteristic of this toxaemia is tissue waste, depending in part on the perverted metabolism, but also on the primary anorexia and consequent relative starvation.

It is altogether a disorder of nutrition. In cases where the anorexia is absent or where the patient has fought against it and taken his food as usual there may be no actual tissue loss. In such cases although the total body weight is retained the tissues, especially the muscles, are soft and flabby and dieting has generally been along wrong lines. That increase or retention of the normal weight can occur with active, stationary, or advancing disease is of itself sufficient proof that selective dieting and not wholesale stuffing is the proper treatment.

Loss in weight, at first, is not as is so commonly supposed a loss of fat. The subcutaneous fat remains with but little alteration in quantity during the earlier stages. The first sign of the nutritional disorder is a defective metabolism of muscle.

The skeletal muscle becomes soft and flabby, myotactic irritability/

irritability sets in consequent on the muscular malnutrition. The same process is going on in the cardiac and nonstriated muscles. Deficient arterial tension and a tendency to constipation is the result. In the alimentary system the toxic poisoning acts on the mucous membranes or on the controlling centres causing anorexia. If the patient gives way to the anorexia actual loss of flesh follows, due perhaps as much to the diminished intake as to the direct action of the toxaemia. With it is associated a feeling of languor and unfitness for muscular exertion, which may partly be nervous in origin, but more probably is referable to the muscular malnutrition. These changes vary and usually are far advanced before the condition is recognised. The primary factor is a malnutrition of the great proteid-holding tissues of the body. Loss of fat follows secondarily on the starvation caused by the anorexia and dyspepsia which gradually supervenes. The dietetic indication in such a case is a direct increase of proteid in the food, relatively to the other constituents. When such a patient is treated for dyspepsia he is put on a carbohydrate diet so as to give his gastric glands a rest. Thus the tissue which is undergoing most waste is deprived of that constituent in the food/

food which is most necessary for rebuilding and making good the waste. The patient is usually treated with Bismuth and various similar remedies, often for no better reason than that they are usually given in gastric catarrh, causing thereby an aggravation of the constipation and causing absorption of the products of intestinal putrefaction and a secondary series of toxic phenomena. Such a condition may exist for long with not much evident change in the primary tubercular lesion. A vicious cycle has been set up by the constipation and dyspepsia which may become independent of the primary lesion. The local condition may from time to time improve or remain quiescent and yet the dyspepsia may remain. Several of the cases under review give histories of long standing dyspepsia treated for years as pure gastro-intestinal disturbances with a great variety of diets and drugs. Most of these cases had advanced physical signs on admission which had probably not developed during the last few months before admission, and owing to their having chronic interstitial changes in the mucous membranes of their alimentary canals, ^{they} reacted badly to the treatment.

Apart from purely nutritional disorder the tubercular toxæmia causes certain peculiarities in the reaction of the heat-regulating mechanism. The control of temperature is but little understood, but/

but, whether we regard the presiding mechanism as a single centre or a series of scattered cells presiding over the metabolism of the various organs, the control and balancing of the generation and dissipation of heat is primarily a function of the nervous system. There is an undoubted relation between nervous instability and tuberculosis, but which is the causal factor we need not stop to consider.

The subject is treated at length in Dr. Clouston's *Neuroses of Development*.

The temperature in phthisis is, perhaps next to the cough the one feature of the disease which is most subjected to independent and empirical treatment. It receives a share of therapeutic attention which would suggest that it was the cause, as well as an outward expression of the activity of the disease. Patients are systematically treated with antipyretics without any direct enquiry as to whether the temperature may not be caused by some extraneous factor, which is capable of alleviation or removal. Healthy metabolism resulting in the release of energy for the supply of the tissue cells is interfered with, by the depressing action of antipyretics, although this interference is less than that caused by the elevation of temperature. The treatment of perturbation of temperature should always be preceded/
ed/

preceeded by an enquiry into the exact pathological factor which has caused it.

The action of the tubercle toxin on the heat-regulating mechanism, as the sum total of the forces controlling metabolism is called, is complex. The researches of Maragliano indicate that there is more than one toxic body concerned in the production of the perturbations.

(Maragliano Berlin. Klin. Woch 1896 page 409).

He used in his experiments a virulent culture of the bacillus filtered to render it sterile and concentrated by evaporation at 30° C. Injection of such a filtrate causes a fall in temperature and sweating. If the same filtrate be heated to 100° C. and this injected, the reverse effect is produced and a rise in temperature results. He infers that there are two substances acting on the heat centre, one of which depresses the temperature while the other raises it. In a filtered culture at 30°C the former is in excess but it is destroyed by a temperature of 100° C thus allowing the temperature-raising ingredient to act. If the same toxic bodies are produced in the intranodular metabolism of the bacillus, this complexity may account for much of the conflicting evidence which confronts one on approaching the subject.

Tuberculosis, pure and simple is essentially a nonpyrexia disease. Cases of surgical tuberculosis e.g./

e.g. hip joint disease do not exhibit any signs of pyrexia until they have been interfered with, and secondary infection introduced. Even in cases of acute pulmonary tuberculosis (Remhold, Ref. Osler page 219) temperature perturbation may be conspicuous by its absence even where a definite diagnosis was made post mortem. These facts would indicate that pyrexia is not a necessary accompaniment of even advancing tuberculosis. It is unusual to meet with such cases but it is significant that they undoubtedly occur. The rise in temperature is in many cases secondary to the toxic action and consequent functional disturbance of various other systems. The heat-regulating centre is exposed to true poisoning by a set of toxins with antagonistic actions. Although their specific actions on the heat centre are antagonistic and may cause no actual disturbance, the one set of toxins throwing the centre ~~one~~ out of gear in the one direction and tending to raise the temperature, the other set throwing it out of gear in the opposite and tending to lower the temperature, the toxin is still a nerve poison. Although a single specific effect is prevented from occurring by this antagonistic action, the cells of the centres are exposed to the action of a poison, the total amount of which equals the sum of the two toxic constituents/

constituents, each having a devitalizing effect on producing the nerve cells and therefore, an increased irritability to external stimuli. Exaggerated response to stimuli is found clinically to be the characteristic of the action of the centre in tuberculosis.

Incidents, which would cause no temperature perturbation in the normal individual, cause an exaggerated response in the tubercular subject. Such a state of affairs may be accounted for by the above explanation. Lauder Brunton (Action of Medicines p 519) attempts to prove that the sweating, which occurs in phthisis and has a close relationship to the pyrexia, is due to the venosity of the blood, from exhaustion of the respiratory centre, stimulating the sweat glands. He found that doses of strychnine controlled the sweating. While it may be true that some of the sweating may be the result of the venosity of the blood, it is probable that it is due in great part also to the disordered action of the heat-regulating mechanism, sweating being one of the methods whereby the heat balance is controlled. May the action of strychnine not be due to the toning up of the nerve cells presiding over the subordinate vasomotor and sweat centres, as ^{it} is found that strychnine also limits the actual swing particularly in these cases in which owing to a primary or induced insufficiency in/

in the action of the central nervous system, the swing is especially exaggerated. The sweating may thus be due to an improper cöordination, if one may put it so, of the various heat-dissipating processes, especially as vasomotor changes, flushings etc, are also almost constantly present, especially with a rising temperature, or at any rate, in close association with temperature perturbation. That tuberculin is found in the sweat is no proof that the sweating is primarily an attempt to eliminate the toxin, any more than the discovery of a toxin in the urine would be a proof that urinary secretion was the same.

It is obvious that the only treatment which will successfully combat such a condition must be directed towards the reduction of the toxaemia and secondarily, to the removal of the incidental causes which precipitate the pyrexial attacks.

In health the daily variation of temperature depends greatly on the occupation and surroundings. It is dependent on the ingestion of food, digestion and the various metabolic changes which occur in its combustion. The temperature is lowered by rest and sleep. The amplitude of the wave varies in different individuals, and in the same individual with differences in work and surroundings. The statement that 98.4 F is the normal temperature simply means that it is the average of the mean daily wave which varies/

varies from about 97.6 to 99.6. The temperature curve may be said to follow the curve of metabolic activity being highest during the working hours of the day and lowest in the early morning when all the vital processes are at the lowest ebb.

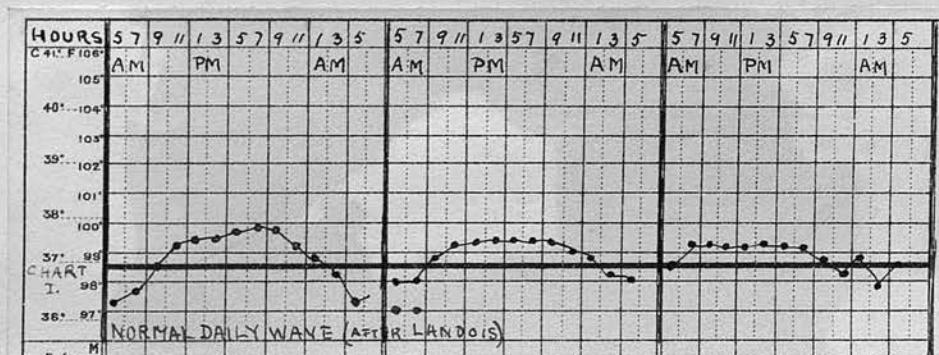


Chart I.

Normal daily wave from three observers (Landois). This being the characteristic of the normal temperature, the commonest characteristic of the tubercular temperature is an exaggeration of the daily wave and exhibits itself as the familiar swinging temperature. The normal and diurnal swing is the expression of the liberation of energy in the form of heat, the extent being kept within physiological limits by the controlling centre acting on the processes of production and dissipation. The swing in tuberculosis is the pathological exaggeration of the same process the disturbing factor being not so much the amount of energy/

energy liberated as the deficient action of the balancing mechanism.

Hence we find that the morning temperature tends to be lower than the normal limit as well as that the evening temperature tends to be higher. If 97.6 F be the physiological limit for a morning temperature it is exceedingly common to find to find in tubercular subjects that the morning temperature is excessively low, when active digestion or other functional metabolic changes are not taking place, owing to malnutrition and feeble metabolism. It is unnecessary to point out the frequency with which the evening rise is excessive as it is perhaps the most familiar feature of the disease. A morning temperature of 96° is quite common, even although it is taken no earlier than 8 a.m. when the lowest point and of the wave is past several hours before, the tissues have entered on another phase of metabolic activity.

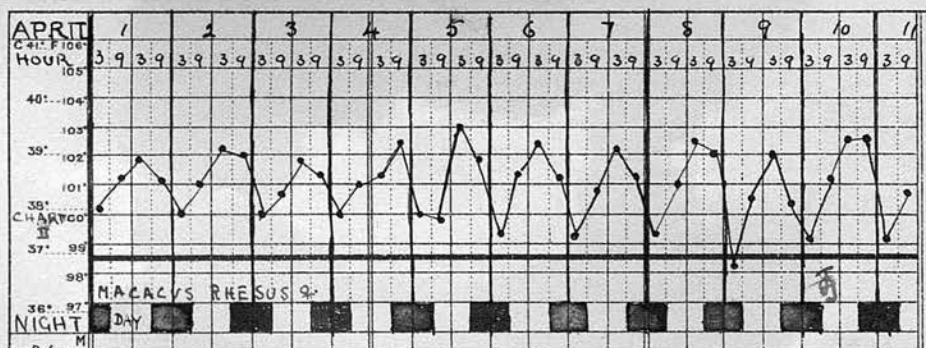


Chart 2
Macacus
Rhesus, ♀

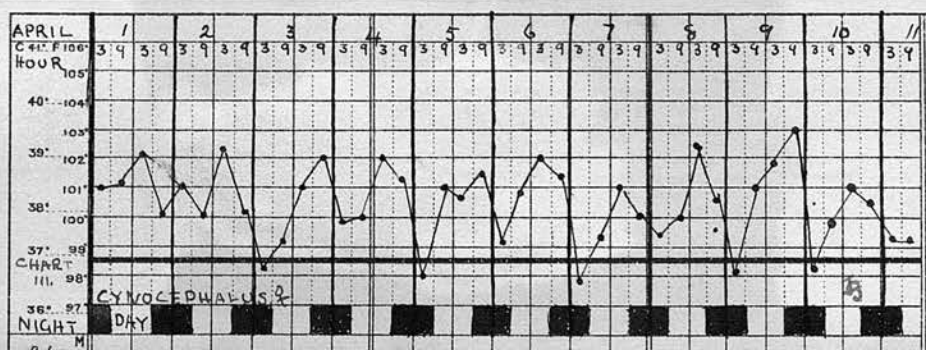
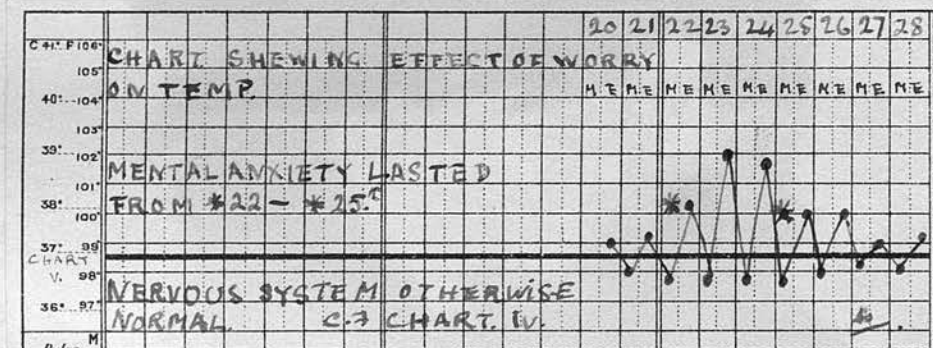
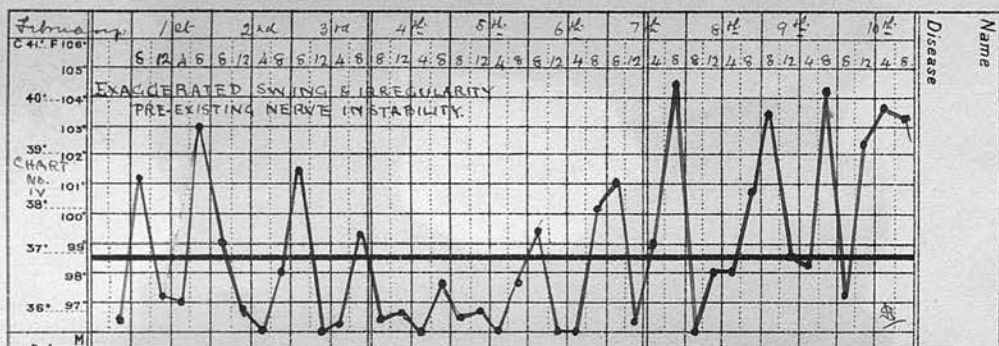


Chart 3
Cyno-
Cephalus. ♀

It is interesting in this connection to note the following chart which shews an excessive swing.

This occurred in a patient with mental disease and consequent excessive nervous instability. The swing was controlled by large doses of strychnine; 5M Liq. Strychnin. thrice daily. In this case the initial weakness of the nerve cells gave an exaggerated effect to the toxic action on the centre, and therefore a response which is exaggerated to an unusual degree.



Apart from the constant daily swing exacerbations are caused frequently by dyspepsia. This acts in the direction of exaggerating the evening rise and in obstinate cases may even persist through the night causing/

The accompanying charts are from a series of observations on the normal temperature wave in monkeys, and the changes produced in it by varying the external conditions. The work is being done by Dr. Sutherland Simpson and myself, in the physiological laboratory of the University. The results are to be published when complete. We have succeeded in proving that the heat-regulating mechanism in the monkey is more susceptible to external stimuli and influences than that of man. It is thus under precisely similar conditions to those which, I hold, influence the action of the heat centres in man, in tuberculosis. The hours represented are 3 and 9. The nights are distinguished by the black band below. The wave resembles a typical advancing case of pulmonary tuberculosis. By selecting the ordinary hospital hours it could have been made even more like a tubercular temperature, but the above hours are chosen so as to cover the 24, and make the chart comparable with that given of the normal and daily wave in man page 66. I have records taken every 2 hours, day and night, of the normal wave in the monkey, extending over several weeks. The above charts are typical examples, but by no means represent the extreme limits of the variation. As in man, the actual amplitude of the wave varies with the individual.

causing a rise of the morning temperature also. It is largely fermentative in origin and is checked in many cases by a proteid diet, which diminishes primary gastric fermentation, as it does not tend to decompose till it reaches the peptone stage when it is rapidly absorbed. Similar temperature disturbances have been shewn to be due to nervous excitement, constipation, septic absorption from decayed teeth etc.

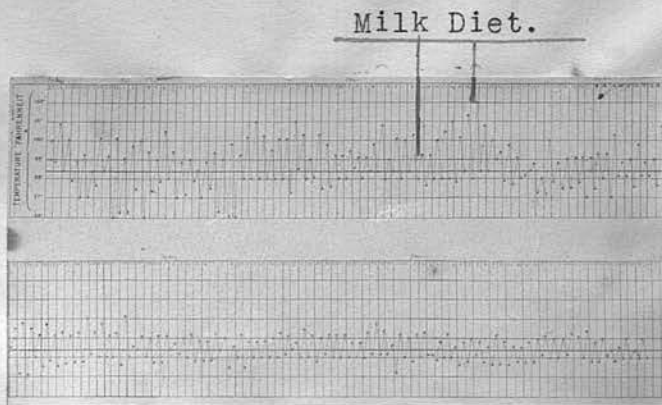



CHART. 6

Chart No.6 is the that of a case of extensive bilateral disease, gastric symptoms were marked. On admission the gastric juice contained no free hydrochloric acid but a large amount of lactic and acetic acid, and large numbers of *Sarcinae*. The patient had been fed on milk and eggs and had been sick several times daily for months. She was put on a meat diet and improved rapidly. The vomiting diminished and finally ceased. The temperature was lowest when no carbohydrate was given, the diet consisting/

consisting of meat and gluten bread. Any attempt to give carbohydrate, especially in the form of milk was followed by an increase in the gastric disturbance and a rise of temperature. Such a period of disturbance is shewn on the chart  page 70 between March 10th and March 17 when the milk was stopped, and the temperature and other symptoms returned to the usual. The disturbance was probably caused by the lactose setting up renewed fermentation. It ^{not} was [^] due to the milk fat as the patient had all along been taking fat in the form of butter. Besides the direct effect of the diet on the temperature the case shews the importance of adhering rigidly to the proteid diet in gastric cases with fermentation. In all the cases whose charts are given, as shewing particularly types of rise, removal of the exciting cause was followed by a fall in the temperature, leaving simply the exaggerated daily metabolic wave.

In a similar manner the temperature curves of intercurrent attacks are exaggerated, so as to obscure the true nature of the condition, and lead to all such attacks being grouped together as Influenza, whether the condition be associated with the presence of organisms or not.

This does not explain a certain class of temperature shewing a constant rise which occurs fairly frequently. As the prime factor in the production of the peculiarities of the temperature in tuberculosis is the toxin, it is probable that variations in the constitution of the toxins may, of themselves, immediately cause actual perturbations.

While a great number of the disturbances of temperature one meets with in the course of the disease are undoubtedly due to secondary causes, there remains a number which are definitely tubercular in origin. As toxin secretion in tuberculosis is a constant process and not intermittent, so the purely tubercular temperature is a constant change, either in the direction of the constant rise, or constant fall.

In practically all other diseases where the temperature rise is produced by toxin secretion, it takes the form of a constant rise or wave. Where an intermittent temperature is present, as in Malaria, it is associated with a periodic metabolic activity on the part of the invading organism. The shape of the temperature waves is often so exact as to be of diagnostic importance, as in the differential diagnosis of measles and scarlet fever. When it is simply due to the organismal toxins it is never intermittent/

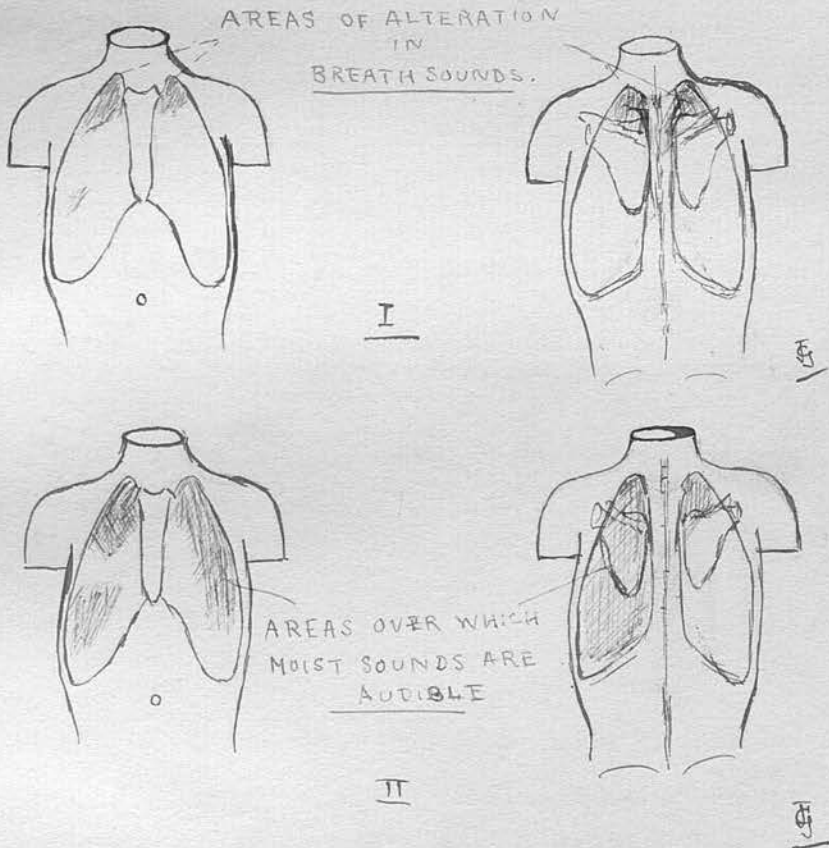
intermittent, except in so far as the daily variation is superimposed on the simple wave. Such a persistent change in the temperature line would occur, either in cases of rapidly advancing disease, with excessive toxic production, or where only slight toxic excretion takes place, and there is a consequent accumulation occurring in the system. My series of cases contains two examples, of the latter, which illustrate this feature. They were both definitely tubercular beyond doubt, and had fairly extensive disease. The striking features of the lesion were that in each case the change in the breath sound was limited to a small area, while moist catarrhal sounds were heard over a much larger area. In one case there was no sputum and in the other only an insignificant amount. They both had a constant pyrexia, the morning temperature rarely falling below normal and, except when influenced by secondary causes, rarely exceeded 100° or $100^{\circ}.5$ at night.

In cases of pyrexia in tuberculosis, where the elevation is due to secondary causes, it quickly yields when the exciting cause has been removed, or where antipyretics have been given. This is a marked contrast to the purely tubercular temperature under discussion. Full physiological doses of antipyretics have practically no effect on its mean height except that they eliminate the secondary metabolic/

metabolic and normal variation. The simple constant rise which in this class of cases is never very great, is totally unaffected by antipyretics. Doses of phenacetin and Salicylate of Soda which would bring down the temperature in an intercurrent influenza, here have no effect, even when continued for weeks. The constant rise in this class of case may be explained by the extensive area, in which the process of toxin secretion is actively taking place, as evidenced by the moist râles heard on auscultation, and the absence of any outlet for toxin excretion. The total amount of toxin elaborated is absorbed owing to there being no sputum. In these cases the anorexia and dyspepsia, which we have all along associated with the systemic action of the tubercle toxin is a marked and persistent feature. A certain part of the temperature disturbance may be due to this secondary cause, but changes in diet produce very little effect so that the digestive disturbance does not account for the whole. The primary lesion is diffuse with only slight consolidation and lymphocytic infiltration and consequently there is excessive systemic toxaemia manifesting itself in the above directions.

These cases shew a tendency to recurrent haemorrhage which is what one would expect seeing that the/

the areas of infection are unsupported by any zone of consolidation. The condition is chronic, not sufficiently rapid to be called miliary, but is rather a poor reaction on the part of the systemic cells. The prognosis in such cases is bad. One of the cases has gone back since leaving the Sanatorium while the other does no more than maintain the improvement. They have both had recurrent haemorrhage both before and after treatment although none occurred while under observation.



Compare the relative sizes of the shaded areas in each pair.

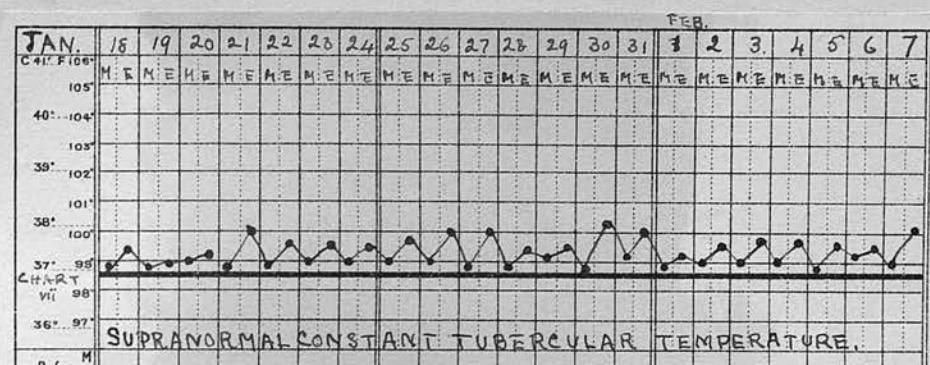


Chart 7 Temperature morning and evening. The highest temperature was about 4 p.m. and the lowest, about 4 a.m. (probably) so that the extreme range of the swing is not evident.

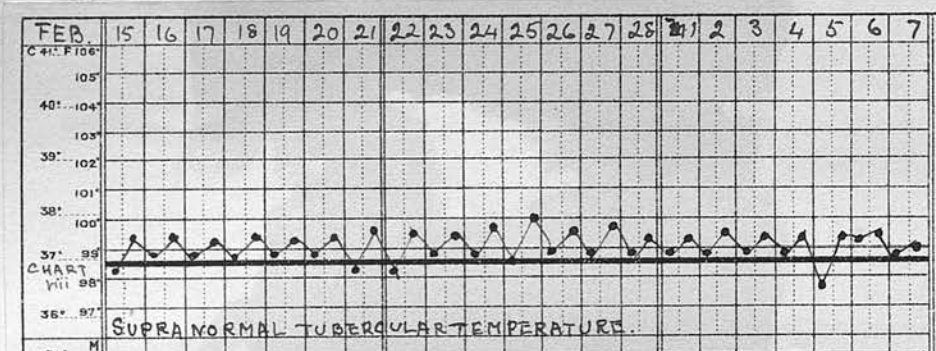


Chart 8 Temperature case whose chest charts are given on page 75, occasionally subnormal.

- I. Chart of chest shewing the area of change in Breath sounds. II areas of catarrhal sounds, in the same patient at the same date.
7. 8. Temperature charts from two cases shewing a typical period. The swing is never great, but rarely subnormal. The curve differs from that of a case progressing favourably in that it is constantly a degree or a degree and a half higher.

The natural method of limitation of the local lesion is in the direction of increased cellular infiltration, thereby shutting in the toxin secreting area with a zone of actively functioning lymphocytes.

The secondary toxic phenomena are roughly divisible into two groups. The one group consists of those functional disturbances which are directly referable to a malnutrition of the muscular system, consisting of a proteid degeneration and subsequent waste more or less depending on the anorexia and dyspepsia. The second group owe their existence to a corresponding functional disorder of the nervous system. This latter group can only be successfully combated by a direct diminution in the systemic toxæmia, this diminution being the result of an improved reaction to the disease and depending on the success of the process of limitation. The former group, while depending on the same phenomena, is of the nature of a vicious cycle having its origin in a nutritional defect which can be directly corrected by appropriate dieting.

Thus the double indication, derived from the study of the pathological process, which we have to guide us in the elaboration of a treatment, is to increase the capacity of the body for bringing about the local arrest, and at the same time to make good the/

the metabolic error. The rational treatment provided that we cannot produce an artificial immunity must be Dietetic.

The production of an artificial immunity or immunizing serum seems to be at present impossible, in view of the complex nature of the toxic bodies concerned. The difficulties have been fully pointed out by Welsh in his recent Huxley lecture alluded to above. The production of an antitubercular serum has been tried by Maragliano, but with indifferent results. What may be achieved in the future is difficult to say, but such seems to be the summary of the present state of affairs. In a disease, whose very name (phthisis) is derived from the malnutrition which it causes, it is evident that the rebuilding of the system must hold a place hardly secondary to that of a curative serum, supposing such a product to exist. If, as I have endeavoured to shew, even the earliest cases are far advanced before there is any chance of recognising the true nature of the trouble, then the importance of the correction of the metabolic error, in order to rebuild the tissues, is still further emphasized. The correction of this error, until serum therapeutics have yielded definitely satisfactory results, will always be the backbone of any successful system of treatment/

treatment, and even after the production of a curative serum, will occupy a place second in importance only to that product. When we have found a line of treatment which will correct the metabolism, and at the same time facilitate the process of encapsulation, we will then have achieved all we can in the way of indirectly combating the disease. The two conditions are fulfilled by a raw or undercooked meat diet. Such a diet fulfills the first indication by producing a large digestive leucocytosis, sometimes almost doubling the number of lymphocytes in the circulation, thereby rendering them directly available for purposes of infiltration. It fulfils the second indication by being rich in the muscle proteids which are undergoing degeneration, and presenting them in the form most easy of assimilation.

Such a form of treatment is not new. It was the essential element in the Salisbury system, but was relatively unsuccessful, principally on account of the absence of the open air element, but partly because it was a hard and fast routine which, being empirical in nature, could not be adapted to the varied requirements of individual cases. It was also carried to extremes, amounting at the start to carbohydrate starvation. Now that it has been revived, as an adjunct to the open air treatment, many of/

of the disadvantages of the old system have been overcome. The fresh air renders a highly nitrogenous diet easy of assimilation, and indeed, necessary. The tendency to digestive disturbances is thereby greatly diminished, while the appetite often exceeds the power of digestion, unless the food be administered in a form easy of digestion and not coagulated by excessive exposure to heat.

The subject of the metabolism in phthisis has been worked at, in this country recently by Goodbody, Bardswell and Chapman. Their researches shew that a tubercular patient tolerates large quantities of proteid food better than a normal individual, and that the quantity of proteid present can be increased to a much greater extent, without giving rise to dyspeptic symptoms. As far as their estimation of the constitution of the diet is concerned their deductions are correct, but, in estimating the actual quantity which should be administered, they omit to take into consideration the fundamental fact, that the digestibility and consequently the capacity for assimilation of food is influenced greatly by the method of preparation. As they make no definite statement to the contrary, it may be assumed that this food was administered cooked. They apparently assume that they have presented the proteid and other constituents of the food to the patient in the form easiest of digestion and assimilation, and, starting from this assumption/

assumption, they administered various dietaries, and proceeded to draw deductions as to the maximum quantity of nitrogen which the patient could elaborate. A large part of their proteid was given in the form of ham, the muscle fibre of which is well known to be less digestible than an equal amount of beef, and at the same time less stimulating. It does not follow that, because a patient only absorbs a certain percentage of nitrogen, the rest passing out unabsorbed in the faeces, on a diet of cooked ham, that the same patient would have absorbed the same percentage on a diet of undercooked or raw beef and that he would suffer the same amount of digestive discomfort. Similarly on a fully cooked diet a larger proportion of the collagen of meat would be hydrated and rendered digestible in the form of gelatin, a proteid which of itself is incapable of sustaining the nitrogen equilibrium, and is therefore of less nutritive value than are ordinary proteids. On a raw or undercooked diet a larger percentage of unabsorbed nitrogen would be in the form of collagen and, even although only the same percentage of nitrogen were absorbed, it would possess a relatively higher nutritive value. In so far as indicating the actual dietetic elements which are best tolerated the paper is of great value.

It/

It shews that proteid and fat are the two elements which are absorbed as well as, or better than, by the normal individual. Of the two the proteid is the more valuable because it is not the aim of treatment to lay in superabundant fat, in preference to muscle. While the function of fat is largely physical, as long as the body is in a state of nutrient equilibrium, the proteid is active in a physiological sense, and partakes in all the processes of vital protoplasmic metabolism. It should therefore be the aim, in rebuilding the tissues, to replace first the more essential element, rather than to replace the non-essential, to the exclusion, in part at least, of the former. The diet must of course include a sufficiency of fat to enable the normal percentage of fat in the tissues to be restored, but beyond that, need not be pushed, especially when it is considered that the fat element in the diet does not actively contribute to the production of the local tissue reaction against the disease. The fact of the proteid being so well tolerated would tend to support the contention raised that:-
 above, the primary metabolic error induced by the toxæmia is a waste and malnutrition of the body proteid.

This contention is also supported by the fact, that in the later stages of the disease, when toxic poisoning /

poisoning has reached its maximum, and emaciation is extreme, the protoplasm of the cells undergoes fatty change, so that there is actual storage of fat in the viscera which would be directly available for metabolism were fat the elementary dietetic constituent which is necessary to restore the metabolism to normal. If fat were essential its presence, infiltrating or otherwise invading the tissues, ought to be a sign of a return to normal, rather than a sign that the toxic process has reached its last stages, ending in collapse of the systemic resistance to the disease.

Apart from the question of absorption and weight increase, we have to consider the effect of diets on the cellular metabolism of the body. That is to say; has diet any special direct action on the tissues? The elementary tissue element, the cell, is the agent employed in resisting disease. The action may be secretory or phagocytic, but the tissue cells, especially the wandering cells, are the agents which are behind and produce the phenomena of reaction to organismal disease. The improvement or otherwise in a condition is directly traceable to the mode in which the cell elements perform their functions. It may be interesting in this relation to quote the remarks of M. M. Henricourt and Richet (*Comptes Rendus. de l'academiei des sciences* 1900 p.608 et seq).

The/

The following is an abstract translation of their communication on the subject of the Raw Beef Treatment of tuberculosis ' We have shewn elsewhere that, in conformity with vague notions, current for some time in medicine, ~~and~~ feeding tubercular animals on raw beef gave remarkable results. We have been able further to follow out the mechanism of this therapeutic action. Cooked meat does not give the same effect as raw. Of two tubercular dogs subjected to a cooked meat diet, the one is dead and the other has lost 17% of its weight. The cooking has probably coagulated certain albuminoid ferments, which are in part if not wholly the active agents in raw meat therapeutics. The muscle pulp and plasma were separately tested. 2 Kilograms of beef is well minced, added to 1 litre of water and left to stand in the cold for 3 hours. The mass is then squeezed, so as to yield 1500 C.C's of a red fluid which gives a coagulum on boiling. This juice is given to two dogs 750 C.C's per day each. The pulp was washed in water for 24 hours, in a current of water to wash away all the residual juice and then pressed. This solid product is called 'Viande Lavee ' The plasma is found to be alone active. (See chart 2.) In consequence, from a therapeutic point of view, in the treatment of tuberculosis, the active principles of/

of the meat are soluble in water. The (control) animals, not so treated are in a state of extreme distress and death is imminent. The raw meat is capable of restoring them to life (Chart II.)

One cannot suppose that this is a case of super-alimentation or even of nutritive value. The muscle plasma acts in another way. 1,000 grams of the plasma contains only 5.3 grams of solid. If it were a case of simple superalimentation the cooked or washed meat should have a greater effect than the plasma.

The contrary is the case. It follows that the immunizing agent is analogous to the cell products of animals injected into the veins. The plasma fixes itself on to the cells of the organism



hindering the development of disease."

Chart I shows the relative specific activity of beef juice as compared with washed pulp (see H. & R.'s paper).

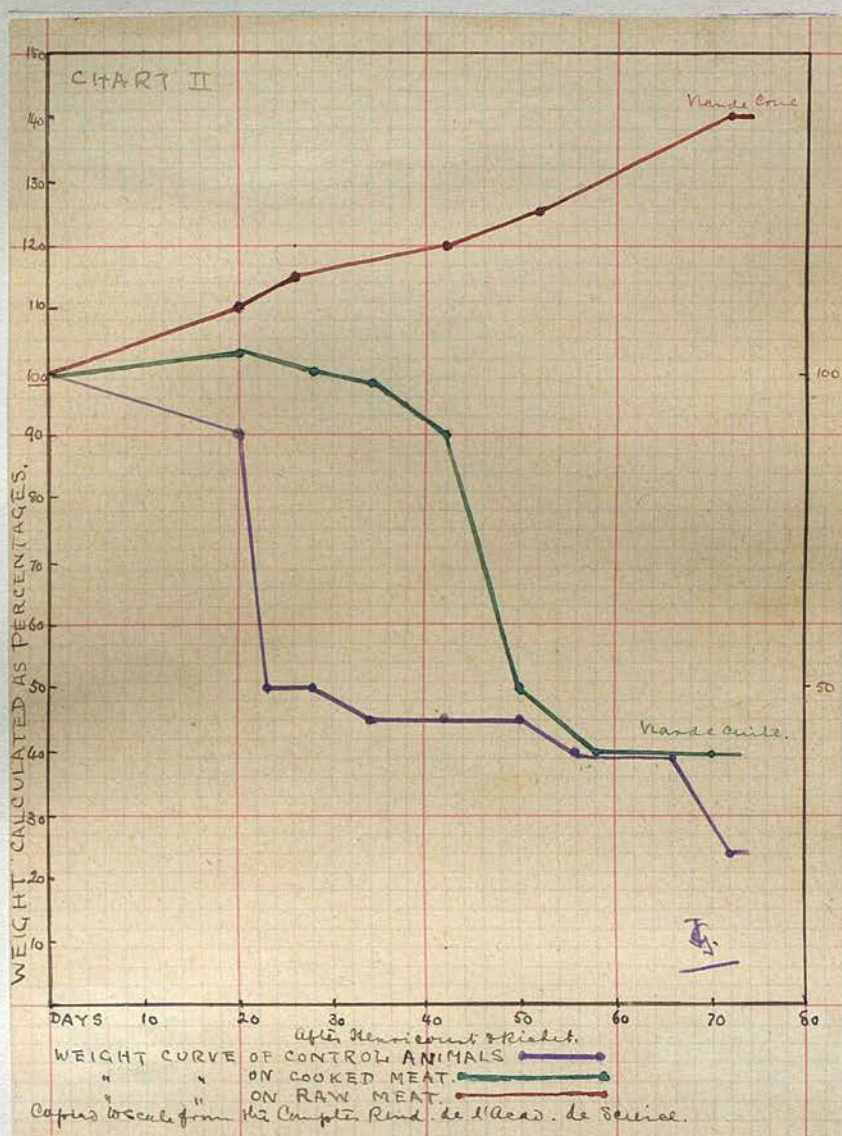


Chart II shews the relative specific activity of raw meat as compared with ordinary diet (control) and cooked meat. The cooked meat and the Viande Lavée, or pulp, practically represent a diet rich in ordinary proteid such as is recommended by Bardswell & Chapman. As compared with raw meat its inferiority, at least experimentally, is evident at a glance. Ordinary proteid can be said in no sense to be a specific in Tuberculosis. Between an ordinary diet and one rich in proteid there is little to choose. The failure of a cooked proteid diet cannot be due, in dogs, to overfeeding. Chart I shews an initial loss of fat as is seen clinically on the commencement of the meat diet.

Such is a summary of the paper of M. M. Henricourt and Richet. The beneficial effect of the juice and raw meat as opposed to ordinary food and cooked meat is undoubted. It perhaps would not be fair to enter into any detailed criticism of their results from such a fragmentary account as is given in the Transactions of the Academy of Sciences, but it is doubtful if their the method of action of explanation of beef juice is correct. Cooking destroys more than the ferments, and the assumption that, because the action is prevented by cooking, it must therefore be due to a ferment, is unwarrantable. Even supposing that the body concerned resembles a toxin or ferment such as is present in serum, it is exceedingly doubtful if such bodies are absorbed unchanged when given by the mouth. (C.F. action of Venene and similar bodies). In any case when such bodies are subjected to digestion and organismal fermentation, taking into account the size of the molecule and the slow rate of absorption, the effect produced by administration by the mouth in tubercular animals would be exceedingly slight as compared with that got by injection into a vein.

The marked reaction got with meat is probably not therefore due to such a meagre absorption of albuminoid bodies. One thing, their researches undoubtedly prove is, that it is not indiscriminate absorption of proteid which is responsible for the action and, that therefore a mere comparison of the ratios/

ratios of absorption and exertion of nitrogen are no certain guide as to the curative value of any diet. They (M.M.Henricourt and Richet) say that the juice only contains soluble products. Prepared as they direct, it contains the nuclein of the tissue as well as the soluble constituents of the plasma. The method is exactly that employed in the extraction of nuclein and nucleic acid from thymus or yeast except that the breaking up of the cells and the extrusion of the nuclei is brought about mechanically by the mincing instead of the chemical action of dilute acids. (Chemical Basis of the Animal Body. Sheridan Lea page 88.)

The practical conclusion to be drawn from the communication is that raw meat, as opposed to cooked, has a specific effect in antagonizing the tubercle toxin. It may be urged that the dog being carnivorous will react better than man, but, as a matter of fact, a dog thrives best on mixed food similar in all respects to the ordinary human dietary.

If the specific action of a raw meat diet does not depend on the absorption unchanged and subsequent action of ferments, what is it due to, and have we any evidence of a specific action on any of the tissues? It is well known that a nitrogenous diet produces changes in the relative numbers of the blood cells/

cells. The state of the blood is of great importance in organismal diseases. It is the fluid tissue concerned in the dissemination of the products of absorption whether these be nutritive or therapeutic in action. It contains the wandering cells which are concerned in the process of resistance to disease, and their secretory products. It is important therefore to investigate the condition of the blood in tuberculosis especially in cases under treatment to discover the effect of the disease on the blood condition, and secondarily the effect of the treatment.

During the years 1900 - 1902 I made a series of observations on the blood condition of patients suffering from pulmonary tuberculosis and treated in the open air on a raw undercooked meat dietary. A summary of the results appeared in a communication to the British Medical Journal March 14th 1903. The paper was entitled the Dietetic Treatment of Pulmonary Tuberculosis from the point of view of Haematology and Histo pathology. A considerable part of the substance of the paper has been recapitulated above in a more elaborate and extended form, but the observations on Haematology have so far not been quoted.

The blood is the only tissue which can be fixed while still alive and undergoing the changes which occur in it in organismal disease and under the influence/

influence of appropriate treatment. The cell elements of the blood and lymph, setting aside the red blood cells which have a definite function, play various parts in the resistance of the body to disease. Whether one holds that the leucocytes function as phagocytes or secretory cells, or as both, the number present in the blood is of equal importance. That all the varieties of leucocyte, although they may have a common origin, have not the same rôle to play is evident from their different behaviour in response to stimuli, thus, the digestive leucocytosis is lymphocytic while that of sepsis is polymorphonuclear.

A marked feature of uncomplicated tuberculosis is the total absence of a leucocytosis. This would seem to indicate a chronic toxic state, where the stimulus is too slight to illicit a response, or what is more likely, a state of equilibrium is gradually produced, the reaction to the poison not exceeding its production. The recuperative power of an individual suffering from pulmonary tuberculosis falls naturally under two headings :- the physiological tissue reaction, which is the primary factor in recovery; and the physical capability of the organ infected for repair. The former, in many cases, is sufficient to stop the advance of the disease/

disease, while the latter may be unable, owing to the extent of the lesion, to bring about a healthy condition with total extirpation of diseased tissue and its replacement by a sound scar. A lung may be so involved as to render this physical shrinkage impossible, for anatomical reasons, even where the physiological reaction has been sufficient to check the advance of the disease. Hence the importance of maintaining the tonicity of the tissues in chronic cases after the active treatment is at an end, and the frequent relapses following apparent recovery. The physical repair is dependent on and necessarily proceeded by the physiological reaction. The benefit of a nitrogenous diet in producing the physiological reaction lies in the production of a general tonicity of the tissues, indicated in the blood by marked changes in the relative numbers of the leucocytes, following the absorption of various constituents of the food, and in the tissues generally by an improvement in nutrition and a gain in weight, which is the indication of an improved metabolism making a physiological use of the food stuffs supplied, rather than the plethoric storage of excess material.

The specific substances which produce the leucocytosis are nuclein and its various derivatives. The leucocytosis so produced is a true increase in the number/

number of lymphocytes in the circulation and therefore of the number of these cells functionally active.

This, as one would expect, entails an increased leucocytic death rate, if one may put it so, and therefore an increased excretion of the products of cellular metabolism. The nuclein derivatives which produce this action, themselves, contain those products, but the increase in excretion is greater than would be accomplished, even were the total quantity of nuclein absorbed and excreted as such.

(Milroy & Malcolm Metabolism of the Nuclein
Journal of Physiology Vol 23 page 229)

To quote from the above observers ' there is absolutely no doubt that nucleic acid (one of the nuclein derivatives) produces a hyperleucocytosis within four hours after its ingestion, and an accompanying or subsequent leucolysis.

The early stages of pulmonary tuberculosis are characterized by the total absence of a leucocytosis, while the later stages invariably shew a leucocytosis, caused probably by the mixed infection. (Clinical Pathology of the blood von Limbeck page 231.)

My observations tend to confirm this statement.

The cases under observation were all advanced cases with cavity formation.

The characteristic features of the blood count were:- /

were:-

- I. A moderate constant leucocytosis.
- II. A large digestive leucocytosis.
- III. A slight but almost constant eosinophilia.

The cases all had subnormal temperatures and in none of them so far as could be ascertained were there intestinal parasites. The morning blood counts, taken fasting at 8 a.m., shewed^a constant slight leucocytosis. The number of leucocytes varied from 10,000 to 14,000. The differential count shewed an increase of the polymorphonuclear leucocytes and to a less extent of the eosinophile cells. The films were prepared in the usual way and fixed in alcohol-ether and stained with Alcoholic Eosin and Methylene Blue. The average percentage was Eosinophiles 2-6 % , Polymorphonuclear neutrophiles 75-80 % , Lymphocytes 18-20 %. These figures give the usual extreme limits of the relative variations in the mornings. They shew an increase of polymorphonuclear cells relatively to lymphocytes. Of the polymorphonuclear cells the eosinophilous variety shewed a slight increase. The digestive leucocytosis was estimated by making a count in the afternoon usually about 4 p.m. The total number of cells shewed a considerable increase. The count varied between 14,000 and 19,000. The differential count shewed/

shewed a great increase of lymphocytes. The usual limits of variation were eosinophilous cells 1-2 %. Polymorphonuclear neutrophiles 55- 66 %. Lymphocytes 30-40 %. Having established the fact that the eosinophile cells diminish, as usual, during digestion, and increase with fasting the differential count was usually made by examination of a film stained with Methylene Blue alone. The digestive lymphocytosis was then estimated by counting all the polymorphonuclear cells (including eosinophilous) and the mononuclear cells and calculating the percentage. Thus the error, if any, lay on the side of over estimating the polymorphonuclear to the extent of about 2 % which was the usual number of eosinophilous cells in the afternoon count. The figures given above shew that the digestive leucocytosis is lymphocytic. Between the two counts the patients had consumed from 12-16 ounces of lean undercooked or raw meat. Only those counts were accepted as correct in which the general appearance of the film corroborated the actual figures. The digestive leucocytosis after a meat diet as is described above is a true increase in the number of lymphocytes circulating in the blood, and therefore of the same cells which possess a direct chemiotactic attraction for the tubercle bacillus and its toxins. The number/

number of cells circulating through the part is thus increased and a greater number of cells are rendered available for the purposes of infiltration and encapsulation of the toxin-secreting area.

In ordinary suppuration the toxins of the invading organisms exert a positive chemiotactic attraction on the polymorphonuclear cells causing invasion of the part by cells which later become pus corpuscles . This process is accompanied, in cases where the reaction against the poison takes place properly, by a leucocytosis, and an increase of the cells in the blood. In tuberculosis a similar attraction acts upon another specific set of cells, the lymphocytes, which end as do the polymorphonuclears of sepsis, in degeneration, which is also of a specific character. Hence, however, the more chronic and slow nature of the process probably prevents any evident increase in the numbers of circulating cells. The two processes differ only in their rate of production, and in the nature of the subsequent degeneration depending directly on the chemical differences between the two sets of toxins. The aim of the raw meat treatment is to call forth an exaggerated response on the part of the specific cells leading to an increasing antitoxic secretion ending in the extrusion of the bacilli. I have noticed that in uncomplicated slight cases, whose complete/

whose complete cure was regarded, on admission, as practically certain, and who reacted most thoroughly and satisfactorily, there was a definite excretion of bacilli in the sputum. While, on admission, in all these cases the bacilli were scanty or absent, within the first six weeks they became exceedingly numerous and the sputum became practically a pure culture. This change was coincident with a diminution of the caseous material in the sputum, with a decrease in quantity, and the substitution of a catarrhal basis full of cells of all sorts, epithelial and connective tissue. The bacilli almost invariably shewed vacuolation, but I have not found this of prognostic significance, as it occurs in sputa of cases of rapidly advancing disease. I have not noticed that apparent clumping and agglutination of the bacilli is of any prognostic value either. So far as I have been able to ascertain the difference of a sputum of a case reacting, and with large numbers of bacilli, from that of a case of progressive disease, is that, while in the latter the bacilli may shew vacuolation or beading, they are always imbedded in a granular caseous matrix which is decolorized with relative difficulty, while in the former, the matrix is uniformly cellular and decolorizes easily, taking up the contrast stain readily. The numbers of bacilli subsequently diminish/

diminish and commonly disappear, when a clear mucoid expectoration replaces the secondary or catarrhal sputum. As to whether the bacilli in such a sputum are dead, I have not had the opportunity of investigating. Less favourable cases with a less pronounced reaction may or may not shew such an excretion, but it was a constant feature of the best type of case.

Where the pathological process is not interfered with by treatment, the antitoxic secretion tends only to equal or to be less than the toxic, so the disease spreads or remains stationary, according as the systemic nutrition is good or bad. Under the extra stimulus of treatment the cell infiltration is probably exaggerated, and the balance swings to the side of increased tissue resistance.

The digestive leucocytosis is probably not produced by the absorption of nitrogenous matter indiscriminately, but by the action of the nuclear constituents. These are the true nucleins, nuclein and nucléic acid.

Chemically they are phosphorized proteids. They are not identical with the nucleoalbumins; when treated with alkalis break up into metaphosphoric acid and a proteid; on metabolism they yield bodies of the Xanthin group, thus differing from caseinogen and other similar nucleoalbumins or pseudonucleins (Schafer's text book of Physiology page 65).

They/

They produce a leucocytosis which the pseudo-nucleins probably do not, and yield an increased phosphorus excretion together with an increase in Uric acid and Xanthin bodies, the latter of which casein does not furnish.

Casein, milk proteid, is a pseudo-nuclein and does not fulfil the required conditions. The leucocytosis is followed by an increase in the products of nuclear metabolism. In the experiments of Bardwell and Chapman on the metabolism in Phthisis quoted above it is stated that in severe cases the excretion of P_2O_5 is small, but in cases with a considerable degree of arrest, amounts to 2.5 and 3 grammes in the 24 hours. This would point to the production of a leucocytosis in successful cases with the 'accompanying or subsequent leucolysis.' Similarly the Uric acid excretion is smallest in these most below weight. In the cases which I investigated the disease was undergoing arrest and the phosphorus excretion was uniformly high amounting to 4-5 grammes in the 24 hours.

As however no estimation was made of the ingested phosphoric acid, no exact conclusions can be drawn, but the facts point to a part, at least, of this large phosphorus excretion being due to the leucocytosis. The difference in the phosphorus excretion/

excretion, in cases of arrest, as compared with the bad cases, together with the remark quoted as to the Uric acid secretion, indicate that the failure in reaction was probably due to the nonproduction of a sufficient leucocytosis. As the primary object is the limitation of the local disease and the secondary object to correct the metabolism, so the effect is probably not simple, but the result of the concomitant action of the two processes. The mere production of a leucocytosis by the administration of pure nucleic derivatives would not suffice in all cases to produce arrest. The correction of the metabolism occupies a part hardly secondary to the leucocytosis.

The production of a tonicity or tissue stimulation by the combination of fresh air and nitrogenous food probably has a deeper than merely nutritive significance, especially in relation to the neutralization and elimination of the circulating toxins. The lymphocytic infiltration may neutralize or furnish constituents to the formation of a neutralizing body for the intracellular necrotic toxins, but it is improbable that it furnishes all the bodies for neutralizing the external toxins.

That cells, other than those of the affected tissue/

tissue or the polymorphonuclear leucocytes, can form, or contribute to the formation of, the antitoxin is known. In tetanus where the formation of the antitoxin is a relatively simple process Wassermann and Takaki have shewn that emulsions of the central nervous system contain bodies with antitoxic properties, and that in certain animals other tissues than that affected, the central nervous system, have the property of combining with the tetanus toxin. In typhoid and cholera whose ^{toxins} ~~tissues~~ are compound and therefore more closely resemble those of tubercle, Wassermann has brought forward evidence that one constituent, the immune body, is produced in the spleen, lymph glands, and bone marrow.* This would seem to indicate that the tissue nutrition has a deeper significance than mere increase in weight and that the selection of a diet should have other objects in view than the single one of increasing weight. *Muir & Ritchie Bacteriology pp 458. 465).

Another fact favouring the view that the lymphocytes are not the only cells concerned is, that the general systemic reaction, shewing itself as an improvement of metabolism and improved functional activity of the muscular system, as evidenced by the state of the circulation and pulse, precedes any change in the physical signs of the pulmonary lesion.

A further improvement in metabolism follows later, consequent on the diminished activity of the tubercular toxin secretion, and subsequent to various alterations in the physical signs.

Leaving for a moment the more theoretical aspect of dieting, it can be shewn that a raw or underdone meat diet has other important physiological actions, which are highly beneficial in their effects on the tubercular subject.

The blood condition tends to be an achromatosis rather than an oligocythaemia, which is what one would expect to have, associated with a state of disordered nutrition. The red blood corpuscles shew relatively little diminution in numbers. A raw meat diet contains all the elements necessary to the restoration of the blood condition to normal.

It contains unaltered the muscle haemoglobin, which is physiologically the source of the greater part of the organic iron, from which the blood pigment is normally manufactured. In addition to the muscle haemoglobin cell nuclei, both animal and vegetable, contain iron. These so called Haematogens together with the muscle haemoglobin are the two chief sources of organic iron (Binge Zeitschrift f. Physiol Chem Strassbourg 1884 Bd IV p.49)

The special advantage in administering the meat,
raw/

raw or as underdone as possible, is that the nucleins and haemoglobin are thereby presented for absorption in the same state of combination as they exist in the body. They cannot of course be absorbed to any great extent unchanged, but the necessary change is thus reduced to a minimum, and the constituents of the complex organic compounds are present in the exact proportion in which they are required in the blood. The number of organic haematinosis almost legion, and they are all recommended for use in tuberculosis. The object in their manufacture is to produce a stable compound not liable to decomposition, in which the iron is held in organic combination and approximates as nearly as possible to haemoglobin. In a meat diet we have these conditions fulfilled in as much as we present the iron compound as haemoglobin, and by the fact that it can be had fresh daily the keeping property is unnecessary and the expense of elaborate preparation is avoided. The effect of the diet on the blood is to produce a large increase in the haemoglobin within a few weeks. The percentage rapidly rises from 50 to 60 per cent on admission to 100 or 130 according to sex. During my observations I have noted that in a case progressing favourably the haemoglobin percentage in a female is always 95-100 while/

while in males it ranges from 118 to 130. Such an increase in the amount of circulating haemoglobin amounting, in many cases, from start to finish, to something over 30-40% must facilitate gaseous interchange thereby diminishing the rapidity of respiration and approximating to that state of physiological rest unattainable in a vital organ.

The rapidity of respiration is probably also affected in the same direction, but by a different method, by a proteid diet. By lowering the relative amount of carbohydrate the respiratory quotient is lowered; less of the oxygen excreted, being in the form of Co_2 and therefore the pulmonary excretion of Co_2 is diminished and respiration slowed.

In this way the actual lung condition is indirectly affected by a proteid diet. In estimating the nutritive effect of the diet on the tissues the fact of the heart being a muscle, suffering from the same toxic malnutrition as the skeletal muscle, must not be lost sight of. The prognosis in pulmonary tuberculosis is more affected, perhaps, within certain limits, by the circulatory condition than by any other factor; especially important is the state of the pulse after the commencement of treatment. We have in it a direct index to the state of nutrition of the cardiac muscle, and therefore an indication as to/

to whether the patient is capable of reacting and taking advantage of the effort to improve his proteid metabolism.

The improvement of the circulation is perhaps the first sign of a reaction. (Philip, British Medical Journal, December 14 1901.)

It is the point at which we come into closest and most intimate contact with the actual muscular metabolism. It precedes the improvement in the local condition, this being the result of a gradual tissue change, while the other is more immediately dependent on the proper performance of nutrition.

The importance of the condition of the muscular system and its malnutrition has been largely lost sight of ⁱⁿ the dieting in tuberculosis. Indiscriminate stuffing can be hardly too strongly condemned, both because of the discomfort it occasions and the ill effects on the digestion of the patient. On ordinary sanatorium diets the patient puts on fat, then has to transform it into muscle, at the expense of considerable metabolic energy, which he can usually ill spare. The breathlessness of the over-fed, or rather improperly fed, consumptive has, in sanatorium circles, become proverbial and has led to a reaction against forced feeding. A diet such as is given in many sanatoria and is of the 'suet pudding variety' tends to the deposition of infiltrating/

infiltrating fat in the heart and viscera. A marked feature of the progress of cases who have been subjected to a diet of this sort, on changing to a meat diet, is a rapid loss of weight, accompanied by a diminution of discomfort, especially of the dyspnoea, succeeded by the deposit of firm muscular substance, and the regaining of the lost weight without any discomfort and with a feeling of vigour and well being, which was conspicuous before by its absence. The question naturally arises, what part in this system is occupied by the open air?

The effects of weather and open air are subtle and vague and so far have not been reduced to order. Taking however the facts which are known, we may say that the open air renders possible the breaking of the vicious metabolic cycle. The fresh air and sunlight are known to increase metabolic activity.

Fresh air stimulates the appetite and diminishes the tendency to the establishment of a state of Plethora, and consequent gastrointestinal disorder. The problem of sanatorium regime is to rest the lung and at the same time to exercise the body and stimulate metabolism. This stimulation is absolutely necessary to gain admission to the system for the food-stuffs necessary to produce the reaction. It is in part produced by the sunlight and open air. Close/

Close rooms tend to the production of anaemia, or achromatosis, with deficient production of haemoglobin, which as we have seen is the characteristic feature of the blood condition. The open air on the other hand facilitates, in some way, the formation of haemoglobin and accounts in part for the excessively high percentages recorded above. It also has other actions on the condition. The temperature steadies in a marked degree and in all cases which are admitted the chart during the first week shews a sudden fall even although a subsequent rise may take place (See chart 6 page 70). The fall in this case may be seen in almost every case. It is attributed to the open air steadying & making more uniform the heat balance, by keeping the surrounding temperature relatively low and at the same time constant. The frequency of respiration is directly diminished and the feeling of oppression and dyspnoea vanishes. The diminished rapidity of pulmonary action is no doubt followed by a change for the better in the local conditions, resulting from the relative state of rest produced. This diminution is due to two factors:- the high and constant percentage of oxygen with a low percentage of impurities and the low temperature of the inspired air. These two causes are known to act in this direction, and probably occasion the immediate improvement./

improvement. A further slowing takes place later as the anaemia is made good. Besides these more obvious effects on nutrition which are matters of common experience and observation, the climatic conditions have an effect on nutrition which has not yet been fully explained. It is dependent not so much on weather as on change of weather, whether this change be in the direction of improvement or the reverse. As long as the weather is constantly the same weight increases tend to be considerable, but changeable weather will cause a loss or diminished increase among all the patients, independently of individual conditions. What the exact factor is it is impossible to say, but the open air has an effect on nutrition which cannot be explained by any of the atmospheric phenomena at present known. By producing this improvement in nutrition the conditions are so altered as to render possible the absorption of sufficient food to produce the desired tissue reaction. The diet and open air are the two main factors in the treatment of tuberculosis, each making possible the therapeutic action and neutralizing the bad effects of the other. Apart from open air, rich dieting cannot be tolerated, together with a rise in temperature, and want of exercise, but the open air renders it possible. On the other hand/

hand the chances of catching cold or other ill effect from the exposure, is prevented by the diet while a direct want is created by the stimulus to metabolic change, which is filled by the increase in the quantity of food which the patient is able and willing to take.

The general appearance of a patient before he commences treatment may be taken as a fair guide to his lung condition, but so marked in the change brought about, in his nutrition, by the diet and open air that by the end of a few weeks it has apparently ceased to bear any relation to the extent of the pulmonary mischief. The first sign of improvement is a diminution in the evident effects of the systemic toxaemia. The muscular system and digestion are the first to react. Dyspeptic symptoms diminish and the circulation improves. Flesh, in contra-distinction to fat, is rapidly put on. The temperature takes somewhat longer to become subnormal the first change being a diminution of the swing, the two extremes gradually approximating to a subnormal line. Sweating in sanatorium practice is practically unknown except in cases where rapid advance is going on, and where the temperature is of the constant supra-normal type. In cases in which the temperature is not definitely tubercular and simply exhibits a swing/

swing, which may be regarded as the evidence of metabolic activity, sweating is unknown and always disappears with the progressive lowering of the temperature which takes place during the first four or five days of the treatment. Where a subsequent rise takes place there is no return of the sweating. As shewn in the 'Metabolism of Phthisis' there is an excess of sweat secretion going on all through which is imperceptible, and appears only in the chemical analysis where the urinary secretion does not bear the proper or usual relationship to the amount of water taken. The sweating, in fact, becomes less in quantity as the toxæmia diminishes, but the change is at first chiefly in the direction of the secretion being less spasmodic from improvement in the nervous control. The sweating is also curiously localized, in some cases, being limited to the head and back of the neck or loins. This is in exact parallel with the localized vasomotor changes:—malar flushings, flushing and swelling of the hands etc, which occur in relation to temperature changes or in relation to outside conditions which tend to alter temperature. Flushings tend to occur with actual temperature change either rise or fall, and in relation to changes in the surrounding temperature, as when patients go into a warm/

Warm room. Localized malar flush with coldness of the extremities is frequently associated with a rising temperature, and local flushings of the extremities when the summit of the wave is reached and during the fall. This would tend to associate the sweatings and flushings with the same cause, as they both occur in relation to temperature change, and are both frequently curiously localized as compared with their physiological occurrence. They are probably both due to the toxic poisoning of the heat-regulating centres which normally act by coördinating the two, and tend to the direction of spasmodic exacerbation of the physiological process, just as the phthisical swinging temperature is a spasmodic exacerbation of the normal diurnal waves.

The only other form of treatment which need be discussed as being founded on physiological and pathological investigation is the cinnamic acid treatment of Landerer.* This treatment has been so frequently described that it is unnecessary to give more than an outline. The cinnamic acid is injected intravenously in alkaline sodium solution finely emulsified with white of egg. The injection is followed by an polymorphonuclear leucocytosis. This is supposed to induce an intense phagocytosis and removal of the caseous tissue with a superinduced/

* (Die behandlung der Tubekulose Mit Zimintsaure 1898)

superinduced Fibrosis round the area. While phagocytosis can accomplish the removal of microscopic particles and bodies, it is ill adapted for the removal of any macroscopic amount of tissue. The subject has been experimentally investigated by Krompecher who found that animals inoculated with virulent tubercle bacilli died in spite of the administration of cinnamic acid, as rapidly as animals inoculated with the same culture who were subjected to no treatment. (Annales de l'Institut Pasteur November 25 1900).

If the success of the cinnamic acid treatment depends on the induction of a phagocytosis, then the most advantageous time, at which the process can act, is during the early stage when the bacilli are lying in the tissues unsurrounded by any nonvascular area, and consequently exposed to phagocytic action. In spite of this, judging by Krompecher's results, the treatment signally fails. How far Landerer's results are attributable to the improved hygienic conditions of patients cannot be determined.

Ewald (Berlin Klin. Wochenschrift May 21st 1900) after trying the treatment, has come to the conclusion that benefit does result but that the percentages of cures is much smaller than that claimed by Landerer. He finds that the cinnamic acid/

acid causes no degeneration of the bacilli, and has no effect on the temperature or night sweats. He also finds that it predisposes to haemoptysis.

This is what one would naturally expect, if the phagocytosis is effective to any appreciable extent in causing the removal of caseous tissue, which, even although it is dead, must give physical support to the pulmonary vessels and prevent the formation of aneurismal dilatations and subsequent haemorrhage.

If the success of the raw meat treatment depends on the increased infiltration we should expect to find that tendency to haemorrhage is diminished owing to the support afforded to vessels by the firm indurated infiltration, supporting vessels and preventing the occurrence of local aneurismal dilatations. In the series of cases on which my observations were made there was history of previous haemorrhage in 26.6% of which as many as 75% were recurrent. In none of the cases was there any recurrence of the haemorrhage after the commencement of the treatment. Under the term haemorrhage I include only these cases in which there was actual free blood in the sputum, and not cases in which there was merely a slight tinging of the sputum, probably the result of superficial oozing from a granulating surface. Tinging of the sputum, a pale pink is probably a good sign, from the point of view of prognosis, as indicating good/

good vascular supply to the granulation tissue lining the cavities, which has undergone a slight superficial ulceration from excessive exercise or some other disturbing cause, inducing a local hyperaemia in the diseased area. Some of the cases who have for one reason or another given up the system after leaving the Sanatorium and before a cure was brought about and have consequently relapsed, haemorrhage has recurred, but, so far as I am aware, no cases which could be said to have reacted properly from the commencement or in which the treatment was persevered with after leaving, have had a recurrence of the haemorrhage. This total immunity from haemorrhage speaks for itself, as an evidence of the practical value of the meat treatment as a direct in agent, stopping the caseous and disintegrative change, which is the causal element in true pulmonary haemorrhage.

Another fact which must be mentioned in regard to the action of a meat diet is that it controls gastric fermentation. In the case whose chart is given on page 70 the gastric symptoms were intense. True mineral acid was absent in the gastric secretion, while the stomach contents contained an immense quantity of sarcinae and other fermentative organisms. Lactic and acetic acid acids were present. The administration/

administration of the smallest amount of carbohydrate was followed by excessive fermentation and flatulence diarrhoea and vomiting. This was accompanied by a rise in temperature which subsided on the carbohydrate being withheld. The rise in temperature invariably followed the administration of carbohydrate probably the result of the fermentation. The administration of a purely proteid diet for a short time in such cases stops carbohydrate fermentation, and results in rendering the stomach relatively sterile.

(Work of the Digestive Glands)

It has been shewn by Pawlow ^ that at least as regards pancreatic secretion, the administration of an excess of any special constituent of the diet induces directly an increase in the requisite digestive ferment. For example an excess of carbohydrate causes a hypersecretion of the amylolytic ferment of the pancreas. Probably the excess of proteid in this instance, directly induces an increased secretion of pepsin and hydrochloric acid, thus directly diminishing fermentation by the antiseptic action of the mineral acid.

The carbohydrate was gradually added to the diet later with no bad results, and the patient made excellent progress and is now practically well. The tendency to fermentation of carbohydrate is always present in cases with well marked dyspeptic symptoms and/

and the effect of a diminution of carbohydrate with an increase of proteid is always in the direction of checking the process, and restoring to normal the gastro-intestinal metabolism.

This seems to be the physiological basis on which the dietetic treatment of tuberculosis, by means of an increase in the proteid of the diet, rests.

It is a double action, depending on the facilitation of the infiltrating and limiting process, which goes on round the focus of infection and at the same time correcting the intestinal and systemic metabolism.

It thus resists the direct advance of the local lesion, and at the same time corrects the morbid processes set agoing by the circulating toxins of the disease.

Without the open air this diet can not be tolerated by the stomach, and attempts to force the feeding apart from it, result in disaster, by aggravating the intestinal disorder which is present in such a large proportion of cases. The open air also acts by lessening the rapidity of respiration and aiding in the elaboration of haemoglobin, thereby further facilitating the gaseous interchange.

The only aspect which remains to be considered, is the question as to whether the rich proteid diet throws any strain on the organs of excretion and what difference, if any, should be made in the diet in cases/

cases with disease of the urinary tract. My series of cases only contained three with albuminuria.

Case I was a patient with post scarlitinal nephritis in whom the pulmonary tubercle had shewn itself shortly after leaving hospital. The nephritis was not very severe and was healing when patient commenced the treatment. There was no oedema or pleuritic effusion. The patient was put on a full meat diet. After 24 hours of milk and carbohydrate diet the urine contained albumin though less than after meat.

The albumin was not present in sufficient quantity for estimation, but had been fairly copious before admission. Within 5 weeks it had entirely disappeared. During this time the patient was taking 16-20oz of beef or mutton per day besides other food, along with 3 pints of milk, except on certain days when a milk diet was given, for purposes of observation. In this case the toxin secretion had ceased, and the kidney lesion was healing, and the albumin diminishing. The meat diet produced a functional increase in the albumin but never to any great extent. The diet, although rich in nitrogen, was diluted in excretion by the 60 ounces of milk so that the concentration of the urine was never great.

Case II/

Case II. This was a case of enuresis in a girl of 12. It was associated with feeble development and rickets. The urine contained pus, with pus and bladder cells, but never any tubercle bacilli, although there were numerous other organisms. There was tenderness over the kidney regions, at one time or another, on both sides. The administration of Sandal wood oil caused an immediate marked increase in the tenderness with a rise of temperature. On stopping the oil the symptoms disappeared. Owing to the age of the patient the diet was modified to the extent of substituting bread and milk supper for the evening dinner. The urine was never markedly alkaline, but never acid and contained a trace of albumen.

As the tubercle bacillus was never actually discovered in the urine, the diagnosis was so far doubtful. The condition however, occurring with extensive pulmonary disease of considerable duration, was probably one of a pyelo - nephritis secondary to a simple cystitis passing backwards. This diagnosis was supported by the fact that the tenderness over the kidneys was intermittent and never severe and by the small amount of albumen. The diet had no apparent ill effect on the urinary condition and the pulmonary lesion improved considerably. The enuresis/

enuresis improved greatly; the period during which the patient could retain urine increased from one hour to four. When last heard of about a year after leaving, progress was maintained in every direction.

Case III. This was a case of extensive bilateral disease, involving almost the whole lung space with violent swinging temperature. Patient had old standing mitral stenosis. Shortly before admission the patients urine was examined and nothing detected. On admission it was found to contain 5 grs to the oz of albumen. The condition was so critical that it was determined to put the patient on milk and beef juice. Respiration was hurried and shallow but not more so than could be accounted for by the chest and cardiac conditions. Urea excretion was high for several days. Suppression of urine set in suddenly with uraemic symptoms; dilatation of the pupils blindness and twitchings. There was no headache. The onset of the suppression was sudden and occurred about the end of the first week. The urine of the previous 24 hours was almost normal in quantity. The patient died of uraemia after 24 hours of total suppression. No cause could be assigned for the nephritis. The condition was recent as there were no fatty or waxy casts ⁱⁿ the deposit. The beef juice was prepared in almost the same way as that used by M. Henricourt and Richet except that a few drops of acid/

acid were added. The concentration would be about the same. According to their estimation the total solids amounted to only $\frac{1}{2}\%$ so that the extra amount of nitrogen would be less than if the diet were wholly milk.

The conclusions one is tempted to arrive at, although the number of cases is too small to dogmatize, are; that, in tuberculosis of the urinary tract, greater latitude can be allowed in dieting than in ordinary acute infections. That a meat diet besides being indicated by the primary condition in such cases has no effect on the amount of albumen present in the urine, nor does it produce any symptoms of irritation in the urinary tract. In simple nephritis where the toxin or other irritant has ceased to act and the condition is healing a meat diet may cause a slight functional increase in the amount of albumen present in the urine, but does not appreciably retard recovery. In the third case the diet given was justified by the extreme urgency of the pulmonary symptoms, which would have probably brought about a fatal result independently of the kidney condition. It is impossible to say whether the exciting causes of the nephritis was still acting or not, as no cause could be definitely assigned. The probability was that the exciting cause was still in/

in operation, because of the acuteness and short duration of the attack, and the immense number of fresh cellular casts in the urinary deposit.

Apart from cases of actual pre-existing kidney mischief a meat diet, even to the amount of 24 ounces per day with 3 pints of milk, never produces functional albuminuria or other sign of urinary irritation or strain, even when administered during periods of years in cases of very extensive pulmonary mischief.

Appendix.

Tabular statement of results of 100 cases, most of which I have had at one time or another under observation, and who have been long enough away from direct supervision to make a statement as to results of any value. In an insidious disease whose onset is usually slow, and where actual extirpation of the diseased focus in many cases is anatomically impossible, it is only these so-called cures which have stood the strain of work and ordinary life for months or years as the case may be that are of any value from a statistical point of view. So called cures of extensive and grave disease after **three** or four months treatment are simply cases of arrest which may at any time relapse. The treatment of such cases requires that a long period of consolidation and building up of the system should take place before the results will/

will bear the test of time, and the stress of daily life work. This is, and must always continue to be, a necessary accompaniment to any treatment, where cure frequently presupposes and necessitates the removal and extirpation of huge masses of diseased tissue, containing living bacilli, which may be rendered quiescent by treatment, but are always ready to assume the aggressive, provided any devitalization of the tissues of the individual take place, by reason of overwork, bad hygienic conditions, or intercurrent disease. Given however, that the individual has sufficient healthy lung space left, to meet his requirements; that contraction after the elimination of the diseased tissue is anatomically possible; and sufficient time to carry out the contraction and elimination, by ordinary physiological methods; within these limits the cure of uncomplicated pulmonary disease is a perfectly simple matter, if the patient understands the common sense principles underlying the system, and is prepared to carry them out. This must be done rigidly at first but gradually the patient can return to ordinary conditions of life, as the structure built up by appropriate treatment is consolidated by time, and gradually becomes strong enough to bear the stress of active life and he thus again becomes a useful member of society, instead of/

of a public burden and a public danger. In slight cases the cure should be absolutely consolidated in about 2 years; severer cases taking proportionately longer. Even in the worst cases arrest is often possible, and the patient can, under proper conditions, enjoy life and make himself to a certain extent useful. The following statistic is compiled thus:- the results are tabulated as complete cures, permanent arrests with the hope of complete recovery provided the patient can carry out the treatment long enough under good hygienic conditions at home, and temporary arrests which may or may not become permanent. The object in thus classifying them is to arrange the figures in such a way that the value of the statistic will increase rather than diminish as time goes on. Thus for example the complete cures will, so far as one can judge by past experience, remain as such. The temporary arrests will in all probability relapse and die. They are therefore in one of the tables classified along with the deaths as unsuccessful results although they are really only so in degree. The permanent relative recoveries will become complete cures in a certain number of cases and will relapse in other cases. This relapse is counteracted by a certain number of cases grouped in the temporary groups becoming either permanently/

permanently arrested or cured. Thus the three groups will remain, their relative numbers, but little affected by time. The patients grouped as temporary arrests in many cases, with ordinary care ~~will~~ live for years, but the extent of the lesion prohibits the hope that complete extirpation can take place and renders them liable to relapse or recurrence, following some temporary lowering of vitality from intercurrent disease or other conditions. The patients grouped as permanent arrests are in many statistics published as complete recoveries. They are such in as much as they have no symptoms of the disease, but are not complete cures in so far as the time which has intervened has not been long enough to enable complete extirpation of the tubercular tissue and bacilli to take place. As long as the patient has physical signs of consolidation indicated by change in the breath sounds over any given area, even although there be no accompaniments, that patient is as far from the end of the cure, as the patient with physical signs over a corresponding area, before treatment, called erroneously an early limited case, is from the commencement of his disease. The sanatorium treatment is in danger of falling into disrepute, because this elementary fact is not recognised and patients are discharged as cured after a few months treatment/

treatment, when cure in such a period is a physical and physiological impossibility. The result of telling a patient who has undergone three or six months treatment that he is cured, is that he goes and does as he pleases, and committing some indiscretion, promptly has a relapse. If the fact were once recognised, that physical signs are no indication of the extent of a lesion, grave fallacies both at the beginning and end of treatment would be exposed, and errors in diagnosis and treatment so far prevented.

The duration of treatment would be shortened by the former, as physicians would come to recognise that diagnosis is possible, before the development of grave physical signs, and treatment would be begun earlier. Its ultimate result would be rendered a hundred-fold more certain, by frankly telling the patient that the disease has been arrested, but time and care are necessary to enable shrinkage and extirpation to take place slowly. Thus the danger of relapse is greatly reduced. It is a physiological impossibility to remove square inches of granulomatous tissue, or caseous matter, as the case may be, in a few months by any process known to us at the present time, and capable of acting in the lung of a patient who has overcome the toxic stages of the disease.

The/

The success of the treatment depends on the capability of the patient for assimilating sufficient proteid food to induce the reaction. Thus, excessive disturbance of the alimentary system is grouped as a complication. Apart from the actual extent of the tuberculosis, the other chief factor influencing the result is the mental state of the patient. If his, (or her), mental state be weak, and he be unable to bring his will power to bear on the task of recovery and artificially inducing a reaction, or if he does not make up his mind to carry through the system as a whole, and looks upon the routine and rules of sanatorium life as something to be evaded, then the prognosis is grave even in cases of relatively early and limited disease. Any such factor in the patient's mental disposition and his attitude to the treatment can justly be classified as a complication. The extent to which it affects the result can best be gauged by reference to the tables. The only other complications which need be mentioned are tubercular affections elsewhere. Alimentary
 Tabes Mesenterica or Tubercular
 tuberculosis, Peritonitis are serious, for the additional reason that they affect the system on whose efficiency the production of the reaction depends. Tubercular laryngitis is not nearly so fatal as commonly supposed.

The/

The statistics are compiled not with the intent of demonstrating the number of certain or probable cures, as with the object of throwing light on the influence which the various pathological factors exert on the duration, course, and prognosis of the disease. Many cases grouped as permanent relative recoveries could quite fairly be classed as cures, as time is the only factor necessary to make cure morally certain. With these introductory remarks and explanations as a preface I merely give the figures which speak for themselves. The hundred cases include the sixty on which I made observations, and who were under my case during the whole period of treatment. The remaining forty were mostly either known to me personally, or under my observation, for longer or shorter periods, during their course of treatment. No cases admitted after 1902 are included as there has not been sufficient time since to test the result to any reliable extent.

Cases admitted from Oct 1899 to April 1902. = 100

- A Cases which were recognised as hopeless on admission and which, if possible, were sent home again, numbered ----- 15 or 15%
- B. Cases in which on admission hope was entertained of arrest or improvement either temporary or permanent numbered ----- 84 or 84%.
- C. In/

- C. In one case there was no subsequent history - 1%
 B. Includes cases of all degrees of severity, from slight to practically hopeless cases.

Of the 84 cases grouped as B :-

- (a) Complete recovery took place in 21 or 25%.
 These patients are in perfect health, at work and living an ordinary life with no symptoms or physical signs.
- (b) Permanent arrest occurred in 29 or 34.5%.
 These include cases which only require time to become perfect cures, and these in which the arrest has been sustained so long as to warrant the hope that, while eradication is physically impossible, cicatrization may continue indefinitely and, given reasonably good hygienic conditions, no relapse is likely to occur.
- (c) Temporary arrest occurred in 10 or 12%.
 Here the arrest was not so perfect as to warrant the opinion that it will be permanent, (taking into consideration the hygienic surroundings in which the patient has to live).
- (d) Death occurred in-----24 or 27.5 %.
 So that, as indicated above, the number of cases in which the disease has been cured or overcome to such an extent that the patient will probably not die of pulmonary tuberculosis is 50 or 59.5%
 The/

The number of cases in which death took place or relapse is feared is 34 or 39.5% of the 84 cases who underwent the treatment.

(e) Tubercular complications occurred in 25 or 29% such

(f) Aggravation of special symptoms to an extent as to warrant their being classed as non-tubercular complications occurred in 49 or 58.3%

(g) Uncomplicated cases 10 or 11.8%.

Of the 25 cases with tubercular complications 16 had also non-tubercular complications.

Of the 25 cases with tubercular complications, the complication was overcome in 12 cases or 48%.

Of these 1 was an absolute recovery.

11 are permanent arrests and on the way to recovery.

13 cases are either dead or probably only temporarily improved.

Of the 13 in which the treatment was unsuccessful the want of success could definitely be said to be due to the complication in 10, to the extent of the lung mischief in 1, and to the operation of both factors in 2.

The tubercular complications included

Meningitis (commencing),	1 case	Result	1 death
Tub. Peritonitis or			
Tabes Mesenterica	2	" "	2 deaths.

Tub. Ostitis	1	Case	Result	1 temporary arrest of lung lesion.
Genito-urinary Tuberculosis	1	"	"	1 permanent arrest of lung mischief.
Ischiorectal Abscess	4	"	"	2 deaths 2 permanent arrest of pul- monary lesion.
Tubercular Laryngitis	14	"	"	1 absolute re- covery of throat condition and Local lesion 7 permanent arrests * 6 deaths.
				*(absolute re- covery of throat condition.)
Empyema	2	"	"	2 permanent arrests of lung mischief.

In the 49 cases with non-tubercular complications
the complication was overcome in 17 cases or 34.7%
of these 4 were complete recoveries and
13 were permanent arrests.

The remaining 32 died, or permanent recovery
is doubtful, = 65.3%

Of these 32 the unsuccessful issue was
due to the complication in 15 or 30%
" " " lung lesion in 7 or 14.3%
" " both in 10 or 20.4%

The/

The complications were;

Nervous in 17 resulting in :-

1 complete recovery	or 5.8%
6 permanent arrests	or 35.2%
4 temporary arrests	or 23.5%
6 deaths	or 35.2%

Alimentary in 15 resulting in :-

3 absolute recoveries	or 20 %
4 permanent arrests	or 26.6%
3 temporary arrests	or 20 %
5 deaths	or 33.3%

Respiratory in 3 resulting in :-

Bronchitis	1 complete recovery
and	1 permanent arrest
Asthma.	1 temporary arrest.

Of the 61 doubtful cases

53 or 88.3% had complications.

8 or 11.6% had no complications.

The 8 uncomplicated cases all made persistent relative recoveries, requiring only time to bring about a completely successful result or a successful result in 100% .

Of the 52 complicated cases

23 had tubercular complications and some of these also had nontubercular, while in :-

31 had nontubercular only, although several had more than one complication, resulting altogether in :-

2 complete recoveries
 18 permanent arrests
 15 temporary arrests
 17 deaths.

The unsuccessful results were mainly in those cases in which there was more than one complication. The cases ranged from cases in which cure was doubtful, to cases where even temporary arrest was doubtful, judged by the lung condition independently of complications.

Thus even in well established disease the success or otherwise of the treatment depends on the prominence of those symptoms directly referable to the toxaemia, rather than to the extent of the primary lesion, though they are to some extent dependent on one another. Hence the importance of directly combating the toxaemia and the metabolic errors introduced by it, alongside of the direct treatment of the local lesion.

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and

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